Original Effective Date: 03/13/2026
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Policy Number: C30342-A

Redemplo (plozasiran)

PRODUCTS AFFECTED

Redemplo (plozasiran)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Familial chylomicronemia syndrome (FCS)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. FAMILIAL CHYLOMICRONEMIA SYNDROME (FCS):
1. Documented diagnosis of Familial Chylomicronemia Syndrome (FCS)
   AND
2. Documentation of ONE of the following:
   (a) Diagnosis confirmed by genetic testing (variants in LPL, apoC-II, GPIHBP1, apoA-V, or LMF1)
   OR
   (b) Recurrent episodes of acute pancreatitis not caused by alcohol or cholelithiasis
   OR
   (c) Recurrent hospitalizations for severe abdominal pain without other explainable cause
   OR
   (d) Childhood pancreatitis
   OR
   (e) Family history of hypertriglyceridemia-induced pancreatitis
   AND
3. Laboratory documentation of member's current fasting triglyceride level ≥10 mmol/L or 880 mg/dL and member is refractory to standard lipid lowering therapy (e.g. statins, omega-3 fatty acids, fibrates, etc.)
   AND
4. Documentation of absence of secondary causes (e.g. alcohol use, uncontrolled type 2 diabetes, medications, and medical conditions known to increase triglycerides)
   AND
5. Documentation of baseline disease activity (e.g., fasting triglyceride level), prescriber evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., frequency of acute pancreatitis, idiopathic abdominal pain, xanthomas, lipemia retinalis, hepatosplenomegaly, etc.)

CONTINUATION OF THERAPY:

A. FAMILIAL CHYLOMICRONEMIA SYNDROME (FCS):
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by decrease in fasting triglyceride level from baseline OR disease stability or improvement of clinical signs and symptoms (e.g., decreased frequency of acute pancreatitis, idiopathic abdominal pain, eruptive xanthomas, lipemia retinalis, hepatosplenomegaly, etc.)

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by a board-certified lipidologist, endocrinologist, cardiologist, gastroenterologist, or pancreatologist

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:
25 mg subcutaneously once every 3 months

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Lipoprotein Lipase Deficiency (LPLD) Agents

FDA-APPROVED USES:
Indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Familial chylomicronemia syndrome (FCS) is a rare, severe genetic disorder characterized by an inability to properly metabolize triglyceride-rich lipoproteins due to dysfunctional or absent lipoprotein lipase (LPL) activity. Mutations in the LPL gene or related cofactors essential for chylomicron clearance, such as APOC2, APOA5, LMF1, and GPIHBP1, result in the accumulation of circulating chylomicrons even during fasting. This leads to extremely high triglyceride levels – often 10 to 100 times above normal – and dramatically increases the risk of acute, recurrent pancreatitis. Patients may present with early-onset symptoms including severe abdominal pain, xanthomas, and hepatosplenomegaly, and the disorder may remain undiagnosed until adulthood despite longstanding biochemical abnormalities.

Epidemiologically, FCS is exceptionally rare, with estimated prevalence ranging from 1 to 10 per million people globally. Many individuals remain undiagnosed despite classic metabolic patterns and recurrent pancreatitis. Those affected often experience a significant decline in quality of life due to chronic pain, dietary restrictions, and repeated hospitalizations for pancreatitis. In the United States, an estimated 6,500 individuals are

living with genetically confirmed or clinically diagnosed FCS, underscoring the condition's status as both rare and substantially burdensome.

Historically, standard therapy consisted mainly of strict very-low-fat diets (≤20 g/day) in combination with conventional triglyceride-lowering agents such as fibrates and omega-3 fatty acids, though these approaches often fail to sufficiently lower triglycerides in true LPL-deficient FCS. Risk reduction for pancreatitis relied almost entirely on aggressive dietary management, with limited pharmacologic success. Recent therapeutic advances have transformed care through the development of agents targeting APOC3, a key regulator of triglyceride metabolism.

Redemplo (plozasiran) has emerged as a significant advancement in the treatment landscape for FCS. As a small-interfering RNA (siRNA) therapy, Redemplo is designed to silence APOC3 mRNA, thereby reducing production of apolipoprotein C-III, a central regulator of triglyceride metabolism. This targeted mechanism offers a novel and highly effective way to address the core metabolic dysfunction in FCS. Both the U.S. Food and Drug Administration (FDA) and Health Canada have approved Redemplo as an adjunct to diet for adults with genetically confirmed or clinically diagnosed FCS, making it the first siRNA therapy authorized for this indication.

The Phase 3 PALISADE study demonstrated that Redemplo produces sustained reductions in triglyceride levels, with median declines ranging from 59% to as high as 80%, far surpassing the effects of placebo. These reductions are clinically meaningful, as lowering triglycerides to safer levels markedly reduces the risk of acute pancreatitis, the most serious and costly complication of FCS. The study also showed Redemplo users experienced fewer pancreatitis episodes than those receiving placebo, reinforcing its role not only as a lipid-lowering agent but also as a therapy with potential to prevent organ-threatening events.

Redemplo also stands out for its convenience: it is self-administered once every three months via subcutaneous injection, offering a far less burdensome regimen compared with other advanced FCS therapies, which may require monthly dosing. Its tolerability profile is generally favorable, with hyperglycemia, headache, nausea, and injection-site reactions being the most common adverse events. This ease of use and safety profile contribute to its suitability as an ongoing, long-term therapy. Compared to competing agents such as Ionis Pharmaceuticals' Tryngolza, emerging analyses suggest Redemplo may offer superior triglyceride reduction and greater pharmacoeconomic benefits due to reduced pancreatitis incidence and less frequent dosing requirements.

Overall, Redemplo represents a major shift in the standard of care for adults with FCS. Where traditional approaches – strict low-fat diets and standard triglyceride-lowering agents – often fail to adequately control triglyceride levels or prevent pancreatitis, Redemplo provides a disease-modifying option that directly targets a key pathogenic pathway. Its

strong clinical efficacy, convenient quarterly dosing, and demonstrated potential to reduce serious complications position Redemplo as a first-line advanced therapy for patients with FCS who require more effective and targeted triglyceride management.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Redemplo (plozasiran) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Redemplo include: No labeled contraindications.

OTHER SPECIAL CONSIDERATIONS:
Instruct patients to adhere to a low-fat diet (less than or equal to 20 grams fat per day) while using Redemplo (plozasiran).

Inject Redemplo subcutaneously into the front of the thigh or abdomen. The outer area of the upper arm can be used as an injection site if a healthcare provider or caregiver administers the injection.

Do not inject Redemplo in an area where the skin is damaged (tender, bruised, red, hard, or cut). Do not inject into areas with scars or stretch marks.

If a dose is missed, administer Redemplo as soon as possible. Resume dosing every 3 months from the date of the most recently administered dose.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Redemplo SOSY 25MG/0.5ML single-dose prefilled syringe

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SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2026