Medical Drug Clinical Criteria

Subject:	Redemplo (plozasiran)		
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Overview

This document addresses the use of Redemplo (plozasiran), an apolipoprotein C-III (apoC-III)-directed small interfering ribonucleic acid (siRNA) approved by the Food and Drug Administration (FDA) as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). Redemplo is administered via subcutaneous injection once every three months.

Familial chylomicronemia syndrome (FCS) is a rare genetic disorder caused by a pathogenic mutation in the lipoprotein lipase (LPL) gene or one of its cofactors [apolipoprotein C-II (APOC2), apolipoprotein A-V (APOA5), high-density lipoprotein binding protein 1 (GP1HBP1), lipase maturation factor 1 (LMF1)]. Deficiency in LPL activity impairs catabolism of triglyceride-rich lipoproteins like chylomicrons. This leads to very severe hypertriglyceridemia that is associated with recurrent episodes of pancreatitis. Management includes limiting dietary fat to less than or equal to 20 grams per day. Drugs approved for lowering triglycerides are generally ineffective in individuals with FCS.

The clinical efficacy of Redemplo was assessed in a randomized, double-blind, placebo-controlled trial in 75 adults with fasting triglyceride levels of ≥880 mg/dL refractory to standard lipid-lowering therapy. FCS was demonstrated by a history of elevated triglyceride levels (>1000 mg/dL on ≥3 prior occasions) in combination with genetic confirmation, evidence of low lipoprotein lipase activity or a clinical diagnosis. In this trial, a clinical diagnosis was defined as recurrent episodes of acute pancreatitis not caused by alcohol or cholelithiasis, recurrent hospitalizations for severe abdominal pain without other explainable cause, childhood pancreatitis or family history of hypertriglyceridemia-induced pancreatitis. Participants were required to adhere to a diet consisting of less than or equal to 20 grams of fat per day. The primary end point was percent change in fasting triglyceride level at 10 months and favored Redemplo compared to placebo.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Redemplo (plozasiran)

Initial requests for Redemplo (plozasiran) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of familial chylomicronemia syndrome; **AND**
III. Documentation is provided that diagnosis has been demonstrated by one of the following (Watts 2025):
    A. Homozygous, compound heterozygous or double heterozygous loss-of-function mutation in *LPL*, *APOC2*, *APOA5*, *GPIHBP1* or *LMF1*; **OR**
    B. History of elevated fasting triglycerides (greater than or equal to 1,000 mg/dL on three occasions) AND one of the following:
        1. Absent or low postheparin lipoprotein lipase activity (<20% of normal value);
        2. Recurrent episodes of acute pancreatitis not caused by alcohol or cholelithiasis;
        3. Recurrent hospitalizations for severe abdominal pain without other explainable cause;

4. Childhood pancreatitis;
5. Family history of hypertriglyceridemia-induced pancreatitis; **AND**

IV. Documentation is provided that individual has a recent (within 90 days) fasting triglyceride level greater than or equal to 500 mg/dL (Grundy 2018); **AND**
V. Individual will be using Redemplo (plozasiran) in combination with a very low-fat diet (less than 20 gm per day of fat).

Continuation requests for Redemplo (plozasiran) may be approved if the following criteria are met:

I. Individual has a diagnosis of familial chylomicronemia syndrome; **AND**
II. Documentation is provided that diagnosis has been demonstrated by one of the following (Watts 2025):
   A. Homozygous, compound heterozygous or double heterozygous loss-of-function mutation in *LPL*, *APOC2*, *APOA5*, *GPIHBP1* or *LMF1*; **OR**
   B. History of elevated fasting triglycerides (greater than or equal to 1,000 mg/dL on three occasions) AND one of the following:
      1. Absent or low postheparin lipoprotein lipase activity (<20% of normal value);
      2. Recurrent episodes of acute pancreatitis not caused by alcohol or cholelithiasis;
      3. Recurrent hospitalizations for severe abdominal pain without other explainable cause;
      4. Childhood pancreatitis;
      5. Family history of hypertriglyceridemia-induced pancreatitis; **AND**
III. Documentation is provided that there is a clinically significant reduction in fasting triglyceride level with Redemplo (plozasiran) therapy; **AND**
IV. Individual is using Redemplo (plozasiran) in combination with a very low-fat diet (less than 20 gm per day of fat).

Redemplo (plozasiran) may not be approved for the following:

I. Use in combination with Tryngolza (olezarsen); **OR**
II. May not be approved when the above criteria are not met and for all other indications.

Approval Duration
Initial: 6 months
Continuation: 1 year

Quantity Limits

Redemplo (plozasiran) Quantity Limit

Drug	Limit
Redemplo (plozasiran) 25 mg/0.5 mL	1 syringe every 3 months

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals [when specified as Redemplo (plozasiran)]
J3490	Unclassified drugs [when specified as Redemplo (plozasiran)]

ICD-10 Diagnosis

E78.3	Hyperchylomicronemia

Document History

New: 12/8/2025

Document History:

- 12/8/2025 – Select Review: New clinical criteria and quantity limit for Redemplo. Administrative update to add documentation. Coding Reviewed: Added HCPCS NOC C9399, J3490 for Redemplo and ICD-10-CM E78.3.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ ADA/AGS/APhA/ASPC/NLA/ PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73:e285–350.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
5. Regmi M, Rehman A. Familial Hyperchylomicronemia Syndrome. StatPearls [Internet]. Updated: August 8, 2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK551655/ Accessed: December 5, 2025.
6. Watts GF, Rosenson RS, Hegele RA, et al. Plozasiran for Managing Persistent Chylomicronemia and Pancreatitis Risk. *N Engl J Med*. 2025;392(2):127-137.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.