New Drug Overview

Redemplo (plozasiran)

PDL Category: Endocrine Metabolic Agents

Introduction

Disease Background:

- Hypertriglyceridemia, associated with an increased risk of cardiovascular events, all-cause mortality, and pancreatitis at triglyceride levels >500mg/dL (especially with triglyceride levels greater than 1,000mg/dL) is a condition described by an abnormal increase of serum triglycerides (fasting serum triglycerides >150mg/dL or non-fasting >175mg/dL) (*Soffer et al 2026*).
  - The following are fasting serum triglyceride (TG) levels classified (*Rosenson and Eckel 2025*):
    - Normal: <150mg/dL.
    - Moderate hypertriglyceridemia: 150 to 499 mg/dL.
    - Moderate to severe hypertriglyceridemia: 500 to 999mg/dL.
    - Severe hypertriglyceridemia: >1000mg/dL.
  - The following are conditions described by very high triglycerides (≥500mg/dL) (*Soffer et al 2026)* :
    - Familial lipoprotein lipase deficiency (also called Frederickson type 1 hyperlipoproteinemia).
    - Familial apoprotein C-II deficiency.
    - Primary simple hypertriglyceridemia (also called Fredrickson Type V hyperlipoproteinemia).
    - Chylomicronemia syndrome (for triglycerides >2,000 mg/dL).
- A triglyceride is composed of an ester of glycerol and 3 fatty acids. They are obtained from the diet but also produced by the liver. Triglycerides from the diet are absorbed by the small intestine and combined into the core of chylomicrons, which transport triglycerides into the bloodstream, among other agents such as very-low density lipoprotein (VLDL). Chylomicrons acquire apoproteins CII, CIII, and E in the lymph and blood (*Soffer et al 2026)* .
  - Hypertriglyceridemia results from a disparity in the production of triglyceride-rich lipoproteins from the liver (VLDL) and intestine (chylomicrons) and removal of triglycerides from both of these lipoproteins and their remnants (*Rosenson and Eckel 2025*).
- Patients with severe hypertriglyceridemia may develop chylomicronemia syndrome (*Rosenson and Eckel 2025*). Chylomicronemia syndrome is described by concomitant clinical symptoms such as abdominal pain, lipemia retinalis, eruptive xanthomas, hepatosplenomegaly, pancreatitis, or lipemic plasma (*Soffer et al 2026)* .
  - Persistent chylomicronemia is described as very high fasting triglyceride levels of >880mg/dL, which significantly increases the risk of recurrent acute pancreatitis (*Watts et al 2025*).
  - The classic reason of this condition is familial chylomicronemia syndrome (FCS), which is an ultra-rare autosomal recessive disorder with a global prevalence of 1 per 100,000 persons to 1 per 1 million persons (*Watts et al 2025*).
    - FCS is described as biallelic pathogenic variants in genes that encode lipoprotein lipase or one of four cofactors that lead to impaired removal of chylomicrons and very low-density lipoproteins (VLDL).
      - Apolipoprotein C-III , mainly produced by the liver, is a major determinant of TG levels. It circulates on the surface of triglyceride-rich lipoproteins such as chylomicrons and VLDLs and increase TG levels in several manners.
      - Disease is confirmed by the presence of biallelic pathogenic variants in FCS-causing genes (i.e., LPL, GPIHBP1, APOA5, APOC2, or LMF1) as detected by an FDA-approved test or a test performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA). However, genetic testing can be difficult to obtain. Alternatively, diagnosis can be made by North American FCS (NAFCS) Score of greater than or equal to 45 or Moulin Score greater than 10 (*Baass et al 2020*, *Hegele et al 2025*).
- Management of hypertriglyceridemia should include lifestyle changes. Fibrates, omega-3 fatty acids, icosapent ethyl, and statins can be considered. (*Soffer et al 2026).* However, minimal benefit is observed with these triglyceride-lowering treatments for patients with FCS (*Watts et al 2025*).

- Redemplo was FDA approved in 2025.

Pharmacology/Usage

- Redemplo (plozasiran) is a small interfering RNA (siRNA) that degrades apolipoprotein C-III (*apoC-III*) mRNA by RNA interference. Plozasiran contains a covalently linked ligand containing three N-acetyl galactosamine (GalNAc) residues to facilitate delivery to hepatocytes.
  - Plozasiran is a siRNA conjugated with GalNAc that degrades the *apoC-III* mRNA through the RNA interference mechanism resulting in reduced levels of hepatic and serum *apoC-III* protein. Reduction of *apoC-III* protein leads to increased clearance of serum triglycerides.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Redemplo (plozasiran)
• As an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS).	✔

(Prescribing information: Redemplo 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Redemplo (plozasiran)	Solution in a single-dose prefilled syringe for Injection: 25mg/0.5ml	SC	25mg subcutaneous (SC) injection once every 3 months.	• Train patients and/or caregivers on proper preparation and administration prior to start of treatment. • Adhere to a low-fat diet (≤20grams fat per day) in conjunction with Redemplo. • Inject SC 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.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				• If a dose is missed, administer as soon as possible. Resume dosing every 3 months from the date of the most recently administered dose. • The impact of severe renal impairment or end stage renal disease is not known. The impact of moderate or severe hepatic impairment is not known.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Redemplo was assessed in a randomized, placebo-controlled, double-blind trial that included adults with genetically confirmed or clinically diagnosed FCS maintained on a low-fat diet (≤20 grams fat per day (Trial 1). Patients were randomized to receive 4 total doses of Redemplo 25mg (N=26) or matching placebo (N=25), injected SC once every 3 months over a 12-month treatment period.
  - The diagnosis of FCS was based on adults with a screening fasting triglycerides (TG) ≥880mg/dL refractory to lipid-lowering therapy, with a history of elevated TG (in excess of 1,000mg/dL at least 3 times), and evidence of FCS by known genotypes, evidence of low lipoprotein lipase activity, or a clinical diagnosis.
  - In this trial, for patients with clinically diagnosed FCS, the inclusion criteria specified at least one of the following: 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.
  - Patient demographics were generally similar across the treatment groups.
    - At enrollment, the percentage of patients with genetic confirmation of FCS was 46% in the Redemplo group compared with 56% in the placebo group; diabetes was 15% in the Redemplo group compared with 32% in the placebo group; and a history of documented acute pancreatitis in the prior 5 years was 54% in the Redemplo group compared with 68% in the placebo group.
    - Patients in the Redemplo and placebo groups were treated with statins (43%), omega-3 fatty acids (29%), fibrates (69%), or no background TG lowering therapies (25%) at study entry.
    - Mean and median fasting TG levels at baseline were 2,311 mg/dL and 2,030 mg/dL, respectively.
  - The primary efficacy endpoint was percent change in fasting triglycerides from baseline at month 10 (average of 2 assessments, 2 to 7 days apart).
    - Results suggested that the median difference between Redemplo and the placebo group in percent change in fasting triglyceride levels from baseline to month 10 was -58.7% ($p<0.0001$).
    - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

	Redemplo 25mg (N=26)		Placebo (pooled) (N=25)		Redemplo 25mg vs placebo
Parameter (mg/dL)	Baseline	% change at month 10	Baseline	% change at month 10	Treatment difference, % change mth 10
Triglycerides	2008	-80	2053	-17	-59 ($p<0.0001$)
Non-HDL-C	279	-39	268	4	-42
LDC-C	24	112	28	20	92
Total ApoB	72	27	79	12	15
ApoB-48	10	-61	11	45	-106

- Over the 12-month treatment period, the numerical incidence of acute pancreatitis in patients treated with Redemplo 25mg was lower compared with placebo (2 [8%] patients in the Redemplo group compared with 5 [20%] patients in the placebo group).

Clinical guidelines

- **2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of dyslipidemia, A report of the American College of Cardiology (ACC)/American Heart Association (AHA) Joint Committee on Clinical Practice Guidelines, developed in collaboration with and endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, Association of Black Cardiologists, American College of Preventive Medicine, American Diabetes Association, American Geriatrics Society, American Pharmacists Association, American Society for Preventive Cardiology, National Lipid Association, and Preventive Cardiovascular Nurses Association** (*Blumenthal et al 2026*).
  - Recommendations for the management of hypertriglyceridemia include:
    - Lifestyle management is recommended as a first-line approach to reduce triglycerides (TG).
    - It is recommended to intensify LDL-C lowering therapy to reduce atherosclerotic cardiovascular risk (ASCVD) risk in adults with clinical ASCVD and LDL-C ≥55mg/dL and non-HDL-C ≥85mg/dL on max tolerated statins with persistently elevated TG levels ≥150 to 999mg/dL.
    - Olezarsen is recommended as adjunct to diet to lower TG levels and reduce the risk of pancreatitis in adults with FCS and fasting TG ≥1000mg/dL.
    - The addition of icosapent ethyl may be reasonable to lower ASCVD risk in adults ≥50 years with clinical ASCVD or with diabetes and ≥1 ASCVD risk factors, with persistently elevated TG levels ≥150 to 499mg/dL and LDL-C<100mg/dL on maximally tolerated statin.
    - Fibric acid derivatives or prescription omega-3 fatty acids are appropriate to lower TG levels and reduce the risk of pancreatitis in adults with severe hypertriglyceridemia and especially with TG levels ≥1000mg/dL despite dietary intervention.
- **Familial chylomicronemia syndrome (FCS): An expert clinical review from the National Lipid Association** (*Javed et al 2025*).
  - FCS generally has an early age of onset and is described as persistent severe hypertriglyceridemia (defined as ≥885mg/dL, or ≥1000mg/dL depending on region and if Systeme International (SI) units are utilized) with no

secondary factors, resistance to conventional lipid-lowering treatments, and a high risk of recurring attacks of acute pancreatitis.
  - There is generally a lack of response to standard treatments, such as fibrates or omega-3 fatty acids.
  - Management should include medical nutrition therapy that entails a very low-fat diet. Generally there is a restriction of fat intake to <10% to 15% of daily calories. In addition, alcohol should be avoided. Monitor fat-soluble vitamins, supplementing as needed so deficiencies do not occur.
  - Olezarsen, at the time of this publication, was the only APOC3 inhibitor FDA approved for FCS, while plozasiran is listed as being in clinical trials. The authors note that these agents "…show great promise."
  - Assess the benefit-risk ratio of medications known to worsen hypertriglyceridemia.
- **American Association of Clinical Endocrinology Clinical Practice Guideline on Pharmacologic management of adults with dyslipidemia** (*Patel et al 2025*).
  - In adults with hypertriglyceridemia (150-499mg/dL) who have cardiovascular disease or who are at increased risk for atherosclerotic cardiovascular disease (ASCVD), the authors suggest using EPA (eicosapentaenoic acid) in addition to statins.
  - There is not sufficient evidence to recommend for or against the use of EPA in adults with severe hypertriglyceridemia (≥500mg/dL)
  - It is recommended against using niacin in addition to usual care in adults with hypertriglyceridemia (150-499mg/dL) who have ASCVD or are at increased risk for ASCVD.
  - There is not sufficient evidence to recommend for or against the use of niacin in adults with severe hypertriglyceridemia (≥500mg/dL)
- **2021 American College of Cardiology (ACC) Expert consensus decision pathway on the management of atherosclerotic cardiovascular disease (ASCVD) risk reduction in patients with persistent hypertriglyceridemia, A Report of the American College of Cardiology Solutions Set Oversight Committee, endorsed by the National Lipid Association** (*Virani et al 2021*).
  - For adults ≥20 years with severe hypertriglyceridemia, triglycerides (TG) ≥500mg/dL and especially with TG ≥1000mg/dL:
    - For either TG level, rule out secondary causes and optimize diet and lifestyle. Emphasize/implement a (very) low-fat diet per TG level.
    - Consider statin initiation or intensification in appropriate groups.
    - Consider fibrate or prescription omega-3 fatty acids (icosapent ethyl or omega-3 acid ethyl esters) to reduce pancreatitis.
- **Consensus statement by the American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) on the management of dyslipidemia and prevention of cardiovascular disease algorithm- 2020 Executive Summary** (*Handelsman et al 2020*).
  - Regarding management of hypertriglyceridemia, lifestyle modification should occur first. This may include reduction of weight or modifying intake of macronutrients, as well as increasing physical activity. In addition, secondary causes of hypertriglyceridemia should be addressed first, such as diabetes or medications that may increase triglycerides.
  - Prescription agents used to reduce triglycerides include fibrates, omega-3 fatty acids, and nicotinic acid (niacin). In addition to primary LDL-C lowering effects, statins and PCSK9 inhibitors can moderately reduce triglycerides, while ezetimibe may have a mild triglyceride-lowering effect.
    - Fibrates are typically thought of as the most potent triglyceride-lowering agent.
    - To reduce acute pancreatitis risk, a fibrate, prescription-grade omega-3 fatty acid, and/or niacin should be provided to all patients with severe hypertriglyceridemia (>500mg/dL).
  - Chylomicronemia, which is generally seen with triglycerides >880mg/dL, requires aggressive triglyceride lowering.
    - This disorder may be a sign of lipoprotein lipase activity deficiency, a manifestation of FCS.

- This disorder is also associated with an increased incidence of acute and chronic pancreatitis.
- Patients with this condition should be seen by a lipid specialist.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:** None.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Redemplo) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included hyperglycemia (12%), headache (8%), nausea (6%), and injection site reaction (6%).

- **Drug interactions:** None.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are not sufficient data on use in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Patients with FCS are at risk for pancreatitis during pregnancy because of defects in lipid metabolism and increased triglyceride levels.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Hypertriglyceridemia, associated with an increased risk of cardiovascular events, all-cause mortality, and pancreatitis at triglyceride levels >500mg/dL (especially with triglyceride levels greater than 1,000mg/dl) is a condition described by an abnormal increase of serum triglycerides (fasting serum triglycerides >150mg/dL or non-fasting >175mg/dL) (*Soffer et al 2026*).
- Patients with severe hypertriglyceridemia may develop chylomicronemia syndrome (*Rosenson and Eckel 2025*).
  - Persistent chylomicronemia is described as very high fasting TG levels of >880mg/dL, which significantly increases the risk of recurrent acute pancreatitis (*Watts et al 2025*).
  - The classic reason of this condition is familial chylomicronemia syndrome (FCS), which is an ultra-rare autosomal recessive disorder with a global prevalence of 1 per 100,000 persons to 1 per 1 million persons.
- Redemplo is an *apoC-III*-directed siRNA indicated as an adjunct to diet to reduce triglycerides in adults with FCS.
- Redemplo is for subcutaneous injection once every 3 months that can be self-administered or administered by a caregiver.
- The efficacy of Redemplo was assessed in a randomized, placebo-controlled, double-blind study that included adults with genetically confirmed or clinically diagnosed FCS maintained on a low-fat diet.
  - The primary endpoint was percent change in fasting triglycerides from baseline at month 10.
    - Results suggested that the median difference between Redemplo 25mg and the placebo group in percent change in fasting triglyceride levels from baseline to month 10 was -58.7% ($p<0.0001$).

- Redemplo was not FDA approved at the time guidelines were published. Guidelines list olezarsen (brand name Tryngolza) as an option, which is also a comparator to Redemplo. Tryngolza is to be administered once monthly as a SC injection while Redemplo provides an alternative less frequent SC dosing (once every 3 months) to Tryngolza.

- It is recommended that Redemplo should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use, given a rare disease indication.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred

References

- Baass A, Paquette M, Bernard S, Hegele RA. Familial chylomicronemia syndrome: an under-recognized cause of severe hypertriglyceridemia. *J Intern Med*. 2020;287(4):340-348.
- Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/ PCNA guideline on the management of dyslipidemia: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2026. [Online ahead of print].
- Handelsman Y, Jellinger PS, Guerin C, 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): 1996-1224.
- 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.
- Javed F, Hegele RA, Garg A, et al. Familial chylomicronemia syndrome: An expert clinical review from the National Lipid Association. *J Clin Lipidol*. 2025; 19:382-403.
- Patel SB, Wyne KL, Afreen S, et al. American Association of Clinical Endocrinology clinical practice guideline on Pharmacologic management of adults with dyslipidemia*. Endocr Pract*. 2025; 31(2): 236-262.
- Redemplo. Package insert. Arrowhead Pharmaceuticals, Inc; November 2025.
- Rosenson RS, Eckel RH. Hypertriglyceridemia in adults: Approach to evaluation. UpToDate Website. Updated February 24, 2025. Accessed June 18, 2026. https://www.uptodate.com.
- Soffer DE, Sciammarella M, Oettgen P, et al. Hypertriglyceridemia. Dynamed Website. Updated April 14, 2026. Accessed June 18, 2026. https://www.dynamed.com.
- Virani SS, Morris PB, Agarwala A, et al. 2021 ACC Expert Consensus Decision pathway on the management of ASCVD risk reduction in patients with persistent hypertriglyceridemia: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2021; 78(9): 960-993.
- Watts GF, Rosenson RS, Hegele RA, et al. Plozasiran for managing persistent chylomicronemia and pancreatitis risk. *NEJM*. 2025; 392(2): 127-137.

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