Familial Chylomicronemia Syndrome (FCS) Agents

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO323

Description

Olezarsen (Tryngolza) is a conjugated antisense oligonucleotide and plozasiran (Redemplo) is a small interfering ribonucleic acid – both are administered subcutaneously.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
olezarsen (Tryngolza)	Adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)	80 mg/0.8 mL autoinjector	0.8 mL/30 days
	Reduction of triglycerides and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG: TG ≥500 mg/dL)	50mg/0.8mL autoinjector	0.8mL/30 days
plozasiran (Redemplo)	Adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)	25 mg/ 0.5 mL prefilled syringe	0.5 mL/90 days

Initial Evaluation

I. **Olezarsen (Tryngolza)** and **plozasiran (Redemplo)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a cardiologist, endocrinologist, gastroenterologist, or provider that specializes in the treatment of lipid disorders (e.g., lipidologist); **AND**
   C. Provider attestation medication will be used in combination with a low-fat diet (i.e., no more than 20 g of total fat per day); **AND**
   D. A diagnosis of one of the following
      1. **Familial chylomicronemia syndrome (FCS); AND**
         i. Diagnosis confirmed by genetic test results such as biallelic pathogenic variants in at least one gene causing familial chylomicronemia syndrome (FCS) (e.g., LPL, GP1HBP1, APOA5, APOC2, or LMF1); **OR**
            a. Provider attestation member has clinical findings strongly supportive of FCS based on <u>one or more</u> of the following:
               i. History of pancreatitis

ii. Recurrent hospitalization for severe abdominal pain without other explainable cause
iii. History of childhood pancreatitis
iv. Family history of hypertriglyceridemia induced acute pancreatitis; **AND**

ii. Documentation member has a pre-treatment fasting triglyceride level greater than, or equal to, 880 mg/dL; **AND**
iii. Provider attestation that the use of traditional lipid lowering medications (e.g., statin, fibrate, omega-3 fatty acid, etc.) has been ineffective in lowering fasting triglyceride level; **AND**
iv. The request is for olezarsen (Tryngolza); **OR**
v. The request is for plozasiran (Redemplo) **AND**
a. Treatment with olezarsen (Tryngolza) has been ineffective, contraindicated, or not tolerated; **OR**

2. **Severe hypertriglyceridemia (sHTG); AND**
i. Documentation member has a pre-treatment fasting triglyceride level greater than, or equal to, 500 mg/dL; **AND**
ii. Treatment with at least one medication from at least **TWO** of the following has been ineffective or not tolerated, or **ALL** are contraindicated:
a. Statin therapy
b. Fibrates
c. Omega-3 Fatty Acid; **AND**
iii. Documentation provider has addressed potential secondary causes of severely elevated triglyceride levels (e.g. alcohol use, CKD, uncontrolled diabetes, medications [atypical antipsychotics, corticosteroids, estrogens, beta-blockers], etc.); **AND**
iv. The request is for olezarsen (Tryngolza)

II. Plozasiran (Redemplo) is considered investigational when used for all other conditions, including but not limited to:
A. Hypertriglyceridemia (any severity)

III. Olzarsen (Tryngolza) is considered investigational when used for all other conditions.

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Documentation member has exhibited a positive clinical response to therapy (e.g. reduction in fasting triglyceride level from baseline, reduction in episodes of acute pancreatitis, etc.); **AND**
IV. Provider attestation medication will be used in combination with a low-fat diet (i.e., no more than 20 g of fat per day); **AND**
V. The request is for olezarsen (Tryngolza); **OR**
VI. The request is for plozasiran (Redemplo) **AND**
    A. Treatment with olezarsen (Tryngolza) has been ineffective, contraindicated, or not tolerated

Supporting Evidence

I. Familial chylomicronemia syndrome (FCS) is a rare genetic disorder characterized by the body's inability to efficiently break down triglycerides due to a lack of functional lipoprotein lipase (LPL), leading to extremely elevated serum triglyceride levels. Diagnosis is confirmed by genetic testing showing the presence of biallelic pathogenic variants FCS-causing genes (e.g., LPL, GP1HBP1, APOA5, APOC2, or LMF1). All genetic variants responsible for FCS have not yet been discovered and there are a significant portion of patients with FCS that have indeterminate genetic results due to uncertain variants (ranges from 20-40%). Foundational organizations have been more accepting of confirmed FCS via a North American Familial Chylomicronemia (NAFCS) score of ≥ 45. The NAFCS is a validated clinical scoring system developed for North American practice to help distinguish FCS from more common causes of severe hypertriglyceridemia when genetic testing is unavailable, delayed, or inconclusive. A score of ≥ 45 indicates that a patient is likely to have FCS rather than multifactorial chylomicronemia syndrome (MCS).
II. Symptoms of FCS include frequent abdominal pain, episodes of acute pancreatitis, nausea/vomiting, and presence of xanthomas and/or lipemia retinalis. Traditional medications used to lower triglycerides are often ineffective in this population. Currently, FCS is managed through dietary intake (less than 20 g of fat intake daily) and other lifestyle interventions (e.g., exercise, avoidance of alcohol, etc.). The goal of treatment is to reduce the risk of acute pancreatitis and avoid long-term organ damage associated with it. There is no specific fasting triglyceride goal for this population of patients. Some literature suggests a goal <750-880 mg/dL is thought to reduce the risk of acute pancreatitis, but there is no consensus on this threshold.
III. Olezarsen (Tryngolza) is indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). Olezarsen (Tryngolza) was studied in a Phase 3, randomized, double-blind, place-controlled trial in 66 adult patients with FCS. Participants had fasting triglyceride levels ≥ 880 mg/dL and they underwent genetic testing to identify variants in FCS-causing genes (e.g., LPL, GP1HBP1, APOA5, APOC2, or LMF1) to confirm the diagnosis of FCS. Patients started a 2-week dietary run-in period (less than 20 g of total fat per day) prior to starting the trial if they weren't already on a stable low-fat diet. The mean age was 45 years old and participants were primarily female and White. The mean baseline fasting triglyceride level was 2630 mg/dL. The primary outcome of mean percent change in fasting triglyceride level from baseline to 6 months was -30% in the olezarsen (Tryngolza) compared to 12% in the placebo

group, difference of -42.5% (95% CI, -69.1 to -17.9). Safety and efficacy has not been established in pediatric patients.

IV. Plozasiran (Redemplo) is a small interfering ribonucleic acid (siRNA) that is conjugated with N-acetylgalactosamine (GaINAc) indicated as adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). Plozasiran (Redemplo) was studied in a Phase 3, randomized, double-blinded, placebo-controlled trial in 75 adult participants with suspected or genetically confirmed FCS. Suspected FCS is defined by at least three separate occasions of fasting TG ≥ 1000 mg/dL and one of the following: recurrent episode of acute pancreatitis, recurrent hospitalization for severe abdominal pain without other explainable cause, or history of childhood pancreatitis. Participants were initially randomized into 25mg and 50mg groups. Participants were then randomized to receive plozasiran (Redemplo) or volume-matching placebo subcutaneously once every three months for 12 months. The mean age was 46 years and participants were primarily female (51%) and white (73%). The median baseline fasting TG level was 2044 mg/dL. Plozasiran (Redemplo) demonstrated a statistically significant difference in TG lowering compared to placebo (difference from placebo of -59% in the 25 mg group and -53% in the 50 mg group) after 12 months of treatment. Changes in TG levels are considered a surrogate endpoint; however, elevated TG levels are correlated with an increasing risk of acute pancreatitis and end organ damage. Plozasiran (Redemplo) demonstrated a greater reduction in acute pancreatitis compared to placebo (two participants in the plozasiran (Redemplo) vs seven in placebo, OR 0.17, p= 0.03).

V. The occurrence of adverse events was similar between both plozasiran (Redemplo) and placebo. The most frequently reported treatment-emergent adverse events included abdominal pain (26%), nasopharyngitis (14%), headache (16%), and nausea (14%). Severe and serious adverse events were less common with plozasiran than with placebo (14% vs 24%) and included elevated AST/ALT levels and hyperglycemia. Discontinuations due to adverse events occurred in three patients in the plozasiran (Redemplo) group.

VI. Given the rarity and complexity of FCS, diagnosis and management should be directed by a specialist such as a cardiologist, endocrinologist, or provider that specializes in the treatment of lipid disorders.

VII. The 2018 Endocrine Practice Clinical Guide for FCS notes standard lipid-lowering medications such an omega-3 fatty acids may be minimally effective and recommend adoption of a very-low-fat diet. Although traditional lipid-lowering medications (e.g., statin, omega-3 fatty acid, fibrate, etc.) are normally ineffective in this population of patients, some triglyceride lowering may be exhibited depending on the patient. Traditional lipid-lowering medications are deemed ineffective if they do not lower triglyceride levels by at least 20%.

VIII. Current standard of care involves lifestyle modifications such as implementing a low-fat diet (e.g., less than 20 g of fat intake daily) and avoiding alcohol consumption and medications known to increase triglyceride levels (e.g., thiazide diuretics, beta-blockers, second-generation antipsychotics, corticosteroids, exogenous estrogen, etc.).

The efficacy of olezarsen (Tryngolza) for severe hypertriglyceridemia was demonstrated in two phase 3, randomized, double-blind, placebo-controlled studies: CORE-TIMI 72a and CORE-TIMI 72b. A total of 1,061 patients were enrolled with fasting triglyceride levels ≥500 mg/dL. Patients

were established and optimized on stable lipid-lowering therapy (i.e. statins, fibrates, and omega-3 fatty acid therapy) prior to enrollment and continued these therapies throughout the duration of the clinical trials; 15% of the participants had a history of pancreatitis in the 10 years prior to study enrollment. Fasting triglyceride levels at baseline were 1,116 (990) mg/dL (CORE-TIMI 72a) and 793 mg/dL (CORE-TIMI 72b). Participants received SC injections of either olezarsen (Tryngolza) 50mg (n = 354), olezarsen (Tryngolza) 80mg (n = 351) or placebo (n = 356) once every 4 weeks for one year. The primary endpoint for both studies was measured as the percent change in fasting triglycerides from baseline compared to placebo at 6 months and 12 months. Compared to placebo, both olezarsen (Tryngolza) groups demonstrated statistically significant decreases in triglyceride levels -62.9% in the olezarsen (Tryngolza) 50mg group (95% CI: -72%, -54%; p<0.0001) and -72.2% (95% CI: -81%, -63% CI; p<0.0001) in the olezarsen (Tryngolza) 80mg group [CORE-TIMI 72a] and -49.2% (95% CI: -60%, -39%; p<0.0001) in the olezarsen (Tryngolza) 50mg group, -54.5% (95% CI: -65%, -44%; p<0.001) in the olesarsen (Tryngolza) 80mg group [CORE-TIMI 72b].

Investigational or Not Medically Necessary Uses

I. Plozasiran (Redemplo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Hypertriglyceridemia (any severity)
      i. Plozasiran (Redemplo) is currently under investigation for the treatment of severe hypertriglyceridemia, and hypertriglyceridemia with atherosclerotic cardiovascular disease. There are multiple trials recruiting that are currently active or completed with results yet to be posted. Requests for this indication are considered experimental and investigational at this time.

References

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4. 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. doi:10.1016/j.jacc.2021.06.011
5. 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–e350.
6. Redemplo (plozasiran) [prescribing information]. Pasadena, CA: Arrowhead Pharmaceuticals Inc; November 2025.
7. 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.
8. Falko JM. Familial Chylomicronemia Syndrome: A Clinical Guide For Endocrinologists. *Endocr Pract*. 2018;24(8):756-763.
9. Marston NA, Bergmark BA, Alexander VJ, et al. Olezarsen for Managing Severe Hypertriglyceridemia and Pancreatitis Risk. *N Eng J Med*. 2026,394:429-441.

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated policy name to Familial Chylomicronemia Syndrome (FCS) Syndrome. Initial length of authorization updated to 12 months. Added criteria for Tryngolza for the treatment of severe hypertriglyceridemia.NAFCS score criteria updated to ask for clinical findings suggestive of FCS.	09/2026
Added new 50mg/0.8mL autoinjector for Trygolza to the QL table	07/2026
Added plozasiran (Redemplo) for the treatment of adults with familial chylomicronemia syndrome and updated the supporting evidence.	05/2026
Added gastroenterologist to required specialist prescriber and added criteria to allow confirmation of FCS via NAFCS score ≥ 45. Updated supporting evidence.	10/2025
Policy created	05/2024