

olezarsen (Tryngolza[®])

Policy # 00941

Original Effective Date: 10/01/2025

Current Effective Date: 10/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of olezarsen (Tryngolza[®])[†] to reduce triglycerides in patients with familial chylomicronemia syndrome (FCS) to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility will be considered for the use of olezarsen (Tryngolza) to reduce triglycerides in patients with familial chylomicronemia syndrome (FCS) when the following criteria are met:

- Patient has a diagnosis of familial chylomicronemia syndrome confirmed by molecular genetic test results demonstrating biallelic pathogenic variants in at least one gene causing familial chylomicronemia syndrome (i.e., lipoprotein lipase [LPL], glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 [GPIHBP1], apolipoprotein A-V [APOA5], apolipoprotein C-II [APOC2], or lipase maturation factor 1 [LMF1]); AND
- Patient is 18 years of age or older; AND
- Patient has a fasting triglyceride level greater than or equal to 880 mg/dL; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has had an inadequate response to standard triglyceride-lowering therapies; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- The requested medication will be used in combination with a low-fat diet (i.e., less than or equal to 20 g of fat per day).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of olezarsen (Tryngolza) when the patient does not have a fasting triglyceride level greater than or equal to 880 mg/dL to be **not medically necessary**.**

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Based on review of available data, the Company considers the use of olezarsen (Tryngolza) when the patient has NOT had an inadequate response to standard triglyceride-lowering therapies to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of olezarsen (Tryngolza) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational**.*

Background/Overview

Tryngolza is the first FDA-approved therapy specifically indicated for adults with familial chylomicronemia syndrome (FCS). It is an apolipoprotein C-III (ApoC-III)-directed antisense oligonucleotide (ASO) that reduces ApoC-III protein levels, thereby enhancing clearance of plasma triglycerides and very low-density lipoprotein. Tryngolza is administered as an 80 mg subcutaneous injection once monthly and is available in a single-dose autoinjector. With appropriate training, patients or caregivers may self-administer the medication. Use of Tryngolza should be accompanied by a strict low-fat diet (≤ 20 grams of fat per day) to optimize therapeutic outcomes.

Familial Chylomicronemia Syndrome

Familial chylomicronemia syndrome (FCS) is a rare, autosomal recessive lipid disorder characterized by severely elevated triglyceride (TG) levels due to biallelic loss-of-function mutations in genes essential for lipoprotein lipase (LPL) activity—most commonly the LPL gene itself. This enzymatic deficiency impairs the breakdown of chylomicrons, leading to TG levels often exceeding 1000 mg/dL. Clinical onset typically occurs in childhood or adolescence and may include recurrent abdominal pain, eruptive xanthomas, hepatosplenomegaly, and neurological symptoms such as difficulty concentrating. The most serious complication is acute pancreatitis, which affects the majority of patients and can be life-threatening.

The primary treatment goal in FCS is to reduce TG levels to alleviate symptoms and minimize the risk of AP. TG concentrations below 750–885 mg/dL are associated with reduced pancreatitis risk. Management relies heavily on strict dietary fat restriction—typically less than 15–20 grams per day—which is difficult to maintain and significantly impacts quality of life. Conventional lipid-lowering therapies such as fibrates, statins, omega-3 fatty acids, and niacin are generally ineffective in FCS. In severe cases, plasmapheresis may be used to manage acute complications.

Due to overlapping clinical features, FCS is often difficult to distinguish from multifactorial chylomicronemia syndrome (MCS), a more common condition driven by polygenic factors and secondary contributors like diabetes or obesity. Accurate differentiation is critical, as FCS is typically unresponsive to conventional lipid-lowering therapies and may require targeted treatment approaches.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Tryngolza is indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome. It was approved in December 2024.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Tryngolza was evaluated in a randomized, double-blind, placebo-controlled clinical trial (Trial 1) involving adult patients with genetically confirmed familial chylomicronemia syndrome (FCS) and severe hypertriglyceridemia (fasting TG $\geq$ 880 mg/dL). Eligible participants were $\geq$ 18 years of age and had documented biallelic pathogenic variants—homozygosity, compound heterozygosity, or double heterozygosity—in one of the five genes associated with FCS (*LPL*, *APOA5*, *APOC2*, *GPIHBP1*, or *LMF1*). A history of acute pancreatitis within the prior 10 years was required for most patients, defined by either a recorded diagnosis or hospitalization for severe abdominal pain consistent with pancreatitis. Enrollment of patients without a definitive history of pancreatitis was capped at 35% of the study population.

All participants were required to follow a low-fat diet ($\leq$ 20 grams/day) during a $\geq$ 4-week run-in period and throughout the study. Patients were randomized in a 1:1 ratio to receive either Tryngolza 80 mg or 50 mg every four weeks (Q4W) via subcutaneous injection. Within each dose cohort, further randomization occurred in a 2:1 ratio to active treatment or placebo. The use of alcohol was discouraged, and dietary counseling was provided throughout the study.

The primary efficacy endpoint was the percent change in fasting triglyceride levels from baseline to Month 6 (average of Weeks 23, 25, and 27). Patients receiving Tryngolza 80 mg experienced a statistically significant reduction in triglycerides compared to placebo (-42.5% ; 95% CI: -74.1% , -10.9% ; $p = 0.0084$). Effects were evident by Month 1 and sustained throughout the study. Additional lipid parameters, including non-HDL cholesterol and ApoB-48, also showed favorable changes with Tryngolza 80 mg.

References

1. Tryngolza [package insert]. Ionis Pharmaceuticals, Inc. Carlsbad, California. Updated December 2024.
2. Tryngolza Drug Evaluation. Express Scripts. Updated January 2025.
3. Tryngolza. New Drug Review. IPD Analytics. Updated January 2025.

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09/04/2025 Medical Policy Committee review

09/10/2025 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 09/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.