MEDICAL MUTUAL®

Drug Policy

Policy:	**20251201**	**Initial Effective Date: 12/18/2025**
Code(s):	**HCPCS J3490, J3590 or J9999**	**Annual Review Date: 12/18/2025**
SUBJECT:	**Tryngolza® (olezarsen)**	**Last Revised Date: 12/18/2025**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

Tryngolza, an apolipoprotein C-III (*APO-III*)-directed antisense oligonucleotide, is indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS).[1] It is recommended to maintain a low-fat diet (≤ 20 grams of fat per day) in conjunction with Tryngolza.

POLICY STATEMENT

This policy involves the use of Tryngolza. Prior authorization is recommended for pharmacy and medical benefit coverage of Tryngolza. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Tryngolza as well as the monitoring required for AEs and long-term efficacy, initial approval requires Tryngolza be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tryngolza is recommended in those who meet the following criteria:

1. **Familial Chylomicronemia Syndrome.**
   Initial therapy: Approve for 6 months if the patient meets ALL of the following (A, B, C, D, and E):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has an untreated fasting triglyceride level ≥ 880 mg/dL*; AND
   C) The patient has undergone genetic testing and meets ONE of the following (i or ii):

i. Molecular genetic test results demonstrate biallelic pathogenic variants in at least one gene causing familial chylomicronemia syndrome*; OR
Note: Examples of genes causing Familial Chylomicronemia Syndrome include 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*).

ii. Molecular genetic test results are inconclusive and the patient has a North American familial chylomicronemia syndrome score ≥ 45*; AND

D) The medication will be used concomitantly with a low-fat diet of less than 10% of calories from fat; AND

E) Medication is prescribed by a cardiologist, an endocrinologist, or a physician who focuses in the treatment of disorders related to severe hypertriglyceridemia.

Patient currently receiving Tryngolza: Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) The patient has demonstrated a positive clinical response with the requested medication*; AND
Note: Examples of response to therapy include reduction in triglyceride level from baseline, reduction in episodes of acute pancreatitis.

C) The medication will be used concomitantly with a low-fat diet of less than 10% of calories from fat; AND

D) Medication is prescribed by a cardiologist, an endocrinologist, or a physician who focuses on the treatment of disorders related to severe hypertriglyceridemia.

Dosing in Tryngolza. *Dosing must meet the following (medical benefit only):*
The recommended dosage of TRYNGOLZA is 80 mg administered subcutaneously once monthly

- Prior to initiation, train patients and/or caregivers on proper preparation and administration of TRYNGOLZA.
- Remove the single-dose autoinjector from the refrigerator 30 minutes prior to the injection and allow to warm to room temperature. Do not use other warming methods.
- Inspect TRYNGOLZA visually for particulate matter prior to administration. The solution should be clear and colorless to yellow. **Do not** use if cloudiness, particulate matter, or discoloration is observed prior to administration.
- Maintain a low-fat diet (≤20g fat per day) in conjunction with TRYNGOLZA.
- Inject TRYNGOLZA subcutaneously into the abdomen or front of the thigh. The back of the upper arm can also be used as an injection site if a healthcare provider or caregiver administers the injection.
- Administer TRYNGOLZA as soon as possible after a missed dose. Resume dosing at monthly intervals from the date of the most recently administered dose.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

Labs/Diagnostics.
Decrease in Platelet Count: TRYNGOLZA can cause reductions in platelet count. In Trial 1, the mean platelet count in the TRYNGOLZA 80 mg group was 188,000 mm3 at baseline, and the mean percent change in platelet count was -10% at Week 53. In comparison, the mean platelet count in the placebo group was 215,000/mm3 at baseline, and the mean

percent change in platelet count was 22% at Week 53. No TRYNGOLZA-treated patient with FCS had a platelet count <50,000/mm3. There were no major bleeding events associated with a low platelet count. Overall, the proportion of patients experiencing a bleeding adverse event was similar across the TRYNGOLZA and placebo treatment groups.

Increase in Glucose: Small increases in average values in fasting glucose (≤17 mg/dL) and HbA1c (<0.2 percentage points) were observed over time with TRYNGOLZA treatment in the FCS population in Trial 1. The incidence of hyperglycemia (defined as adverse events, new antidiabetic medication, or laboratory values) was higher in olezarsen-treated patients without a medical history of diabetes at baseline (52%) compared to placebo-treated patients (35%).

Increase in Liver Enzymes: Increases from baseline in liver enzymes within the normal range were observed with olezarsen treatment in the FCS population. These increases occurred within the first 3 months of treatment and stabilized. Liver enzymes returned towards baseline with discontinuation of olezarsen.

Increase in LDL-cholesterol: Increases in low-density lipoprotein cholesterol (LDL-C) and total apolipoprotein B (apoB) were observed in the FCS population treated with TRYNGOLZA compared to those treated with placebo [see Clinical Studies (14)]. Despite increases in LDL-C, the maximum LDLC value remained low for most patients (i.e., <70 mg/dL for 74% of patients treated with TRYNGOLZA).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tryngolza has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Hypertriglyceridemia (in the absence of a confirmed diagnosis of familial chylomicronemia syndrome).** A trial evaluated Tryngolza in patients with either moderate hypertriglyceridemia and elevated cardiovascular risk or with severe hypertriglyceridemia.5 However, Tryngolza is not FDA-approved for this use.1

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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Drug Policy

REFERENCES

1. Tryngolza™ subcutaneous injection [prescribing information]. Carlsbad, CA: Ionis; December 2024.
2. Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al, for the Balance investigators. Olezarsen, acute pancreatitis, and familial chylomicronemia syndrome. *N Engl J Med*. 2024;390(19):1781-1792.
3. Moulin P, Dufour R, Averna M, et al. Identification and diagnosis of patients with familial chylomicronaemia syndrome (FCS): expert panel recommendations and proposal of an "FCS score". *Atherosclerosis*. 2018;275:265-272.
4. 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*. 2024 Nov 12. [Online ahead of print].
5. Bergmark BA, Marston NA, Prohaska RA, et al, for the Bridge-TIMI73 investigators. Olesarsen for hypertriglyceridemia in patients at high cardiovascular risk. *N Engl J Med*. 2024;390(19):1770-1780.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes J3490 and J3590 or J9999

†When *unclassified drugs* (J3490) or *unclassified biologics* (J3590) or *unclassified antineoplastics* (J9999) is determined to be Tryngolza

Edits and Denials:

Prior approval: Prior approval is required for Tryngolza **(HCPCS Codes J3490 , J3590, J9999)**. Requests for prior approval will be authorized by a nurse reviewer if submitted documentation meets criteria outlined within the Corporate Medical Policy.

Requests for prior approval will be forwarded to a qualified physician reviewer if submitted documentation does not meet criteria outlined within Corporate Medical Policy.

TOPPS: Claims received with **HCPCS Codes J3490, J3590, J9999** will pend with **Remark Code M3M or M4M** and will be adjudicated in accordance with the Corporate Medical Policy.

Liability: A participating provider will be required to write off charges denied as not medically necessary.

HCPCS Code(s):	
J3490	Unclassified drugs
J3590	Unclassified biologics
J9999	Unclassified antineoplastics