| Pharmacy Policy Bulletin: J-1440 Tryngolza (olezarsen) – Commercial and Healthcare Reform | |
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| **Number:** J-1440 | **Category:** Prior Authorization |
| **Line(s) of Business:**<br>☒ Commercial<br>☒ Healthcare Reform<br>☐ Medicare | **Benefit(s):**<br>**Commercial:**<br>**Prior Authorization (1.):**<br>**1.** Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization<br><br>**Healthcare Reform:** Not Applicable |
| **Region(s):**<br>☒ All<br>☐ Delaware<br>☐ New York<br>☐ Pennsylvania<br>☐ West Virginia | **Additional Restriction(s):**<br>None |
| **Version:** J-1440-001 | **Original Date:** 01/29/2025 |
| **Effective Date:** 02/26/2025 | **Review Date:** 01/29/2025 |

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| **Drugs Product(s):** | • Tryngolza (olezarsen) |
| **FDA-Approved Indication(s):** | • Adjunct to diet to reduce triglycerides (TG) in adults with familial chylomicronemia syndrome (FCS). |

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| **Background:** | • Tryngolza is a self-administered, subcutaneous (SC) apolipoprotein C-III (apoC-III)-directed antisense oligonucleotide (ASO).<br>• Tryngolza binds to apoC-III messenger ribonucleic acid (mRNA) leading to mRNA degradation and resulting in a reduction in serum apoC-III protein. Reduction of apoC-III protein leads to increased clearance of plasma TGs and very low-density lipoprotein (VLDL). ApoC-III is a protein synthesized in the liver and intestine that regulates TG metabolism.<br>• FCS is a rare, genetic disorder characterized by extremely high levels of TGs in the bloodstream. FCS prevents the body from breaking down fats consumed through diet due to an impaired function of the enzyme lipoprotein lipase (LPL). TGs are the most common form of fat in the blood. Normal TG levels are less than 150 mg/dL and levels above 500 mg/dL are considered severely high. People with FCS often have TG levels of more than 800 mg/dL. Elevated TGs can cause several complications in patients, the most serious being episodes of acute pancreatitis. Other complications include abdominal pain and fatty deposits in the skin (xanthomas).<br>• Extremely restricted, very-low-fat diet involves limiting daily fat intake to less than 15 to 20 grams (less than 10-15% of total daily calories). Avoid alcohol and simple, refined carbohydrates.<br>• The FCSNext genetic test diagnoses FCS by detecting mutations in the LPL gene or genes.<br>• FCS is diagnosed based on fasting triglyceride levels above or 750 mg/dL (8.5 mmol/L), which do not respond to standard lipid-lowering therapy. The high triglyceride levels lead to symptoms such as severe abdominal pain, |

inflammation of the pancreas (acute pancreatitis), and fatty deposits in the skin. Lipemia retinalis may occur, a condition in which the retinal veins of the eyes appear milky.
- 880 mg/dL to align with the inclusion criteria within the studies.
- FCS is caused by biallelic pathogenic variants in five known genes (specifically, lipoprotein lipase (*LPL*), glycosylphosphatidylinositol-anchored high-density lipoprotein (HDL)-binding protein 1 (*GPIHBP1*), apolipoprotein A-V (*APOA5*), apolipoprotein C-II (*APOC2*), or lipase maturation factor 1 (*LMF1*)).

**FCS Score Diagnostic Criteria (for patients with Fasting TGs > 885 mg/dL**

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| Fasting TG levels > 885 mg/dL for three consecutive blood analyses (measured at least 1 month apart; presence of eruptive xanthoma may be used as a surrogate for high TG levels): **(+5)**<br>Fasting TG levels > 1,770 mg/dL at least once: **(+1)** |
| Previous TG levels < 177 mg/dL: **(-5)** |
| No secondary factor (specifically, alcohol, diabetes, metabolic syndrome, hypothyroidism, steroid therapy, and additional drugs; exceptions include pregnancy and ethinyl estradiol; if diagnosis is made during pregnancy, a second assessment is necessary to confirm diagnosis postpartum): **(+2)** |
| History of pancreatitis: **(+1)** |
| Unexplained recurrent abdominal pain: **(+1)** |
| No history of familial combined hyperlipidemia: **(+1)** |
| No response (TG decrease < 20%) to hypolipidemic treatment: **(+1)** |
| Onset of symptoms age:<br>< 40 years: **(+1)**<br>< 20 years: **(+2)**<br>< 10 years: **(+3)** |

- Numbers in parentheses = weighting given to the presence of each item. FCS score = the sum of all items present. An FCS score ≥10 indicates FCS is very likely.
- A North America Familial Chylomicronemia Syndrome (NAFCS) score ≥ 45 indicates FCS to be very likely.
- ICD-10: E78.3 “Hyperchylomicronemia” may apply to Tryngolza; however, the prescriber must confirm that the member has a specific diagnosis of FCS.
- A 6 month initial authorization is recommended to assess reduction in triglycerides.
- Prescribing Considerations:
    - The recommended dose is 80 mg administered once monthly 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.

## Approval Criteria

**I. Initial Authorization**

When a benefit, coverage of Tryngolza may be approved when all of the following criteria are met **(A. through D.)**:

**A.** The member is 18 years of age or older.

**B.** The member has a diagnosis of FCS (No ICD-10 code), determined by one (1) of the following **(1. or 2.):**

**1.** Genetic test demonstrating biallelic pathogenic variants in at least one (1) gene causing FCS (for example, *LPL, GPIHBP1, APOA5, APOC2, LMF1*).

**2.** Genetic test results are inconclusive, and the member meets one (1) one of the following criteria **(a. through e.):**

**a.** FCS score ≥ 10.

**b.** NAFCS score ≥ 45.
**c.** History of pancreatitis.
**d.** History of eruptive xanthomas.
**e.** History of lipemia retinalis.

**C.** The prescriber provides documentation the member has a fasting triglyceride level ≥ 880 mg/dL.
**D.** The prescriber attests the member will use Tryngolza in combination with diet.

**II. Reauthorization**
When a benefit, reauthorization of Tryngolza may be approved when the following criterion is met **(A.)**:
**A.** The prescriber provides documentation of improvement in triglycerides from baseline.

**III.** An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

## Limitations of Coverage

**I.** Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
**II.** For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

## Authorization Duration

**Initial Authorization**

- Commercial and HCR Plans: If approved, up to a 6 month authorization may be granted.

**Reauthorization**

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

## Automatic Approval Criteria

None.

**References:**

1. Tryngolza [package insert]. Carlsbad, CA: Ionis Pharmaceuticals Inc.; December 2024.
2. Tryngolza (olezarsen) approved in the U.S. as first-ever treatment for adults living with familial chylomicronemia syndrome as adjunct to diet. Bio Space. Available at: https://www.biospace.com/press-releases/tryngolza-olezarsen-approved-in-u-s-as-first-ever-treatment-for-adults-living-with-familial-chylomicronemia-syndrome-as-an-adjunct-to-diet. Accessed December 29, 2024.
3. FDA approves drug to reduce triglycerides in adult patients with familial chylomicronemia syndrome. U.S. Food & Drug Administration. Available at: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-drug-reduce-triglycerides-adult-patients-familial-chylomicronemia-syndrome. Accessed December 29, 2024.
4. Falko, J. Familial Chylomicronemia Syndrome: A Clinical Guide for Endocrinologists. *Endocrine Practice*. 2018; 24:756-763.
5. Familial Chylomicronemia Syndrome. Endocrine Society. Available at: https://www.endocrine.org/patient-engagement/endocrine-library/familial-chylomicronemia-syndrome. Accessed December 29, 2024.

6. Familial Chylomicronemia Syndrome (FCS). The National Pancreas Foundation. Available at: https://pancreasfoundation.org/pancreas-disease/fcs/. Accessed January 15, 2025.
7. Regmi M, Rehman A. Familial Hyperchylomicronemia Syndrome. Available at: https://www.ncbi.nlm.nih.gov/books/NBK551655/. Accessed January 17, 2025.
8. Moulin P, Dufour R, Averna M, et al. Identification and diagnosis of patients with familial chylomicronemia syndrome (FCS): expert panel recommendations and proposal of an “FCS score”. *Atherosclerosis*. 2018;275:265-272.

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