Clinical Policy: Olezarsen (Tryngolza)

Reference Number: PA.CP.PHAR.689
Effective Date: 03/2025
Last Review Date: 02/2025

Description

Olezarsen (Tryngolza™) is an *APOC-III*-directed antisense oligonucleotide (ASO).

FDA Approved Indication(s)

Tryngolza is indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Tryngolza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Familial Chylomicronemia Syndrome (must meet all)**:**

1. Diagnosis of FCS as evidenced by both of the following (a and b, *see Appendix D*):
   a. Fasting triglycerides ≥ 880 mg/dL or ≥ 10 mmol/L (lab must be dated within 90 days);
   b. Genetic testing confirms the presence of a loss-of-function mutation in a FCS-causing gene (e.g., LPL, APOC2, APOA5, GPIHBP1, LMF1);
2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
3. Age ≥ 18 years;

Dose does not exceed 80 mg per month.
Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Familial Chylomicronemia Syndrome (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by reduction in fasting triglycerides from baseline;
3. If request is for a dose increase, new dose does not exceed 80 mg per month.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

APOC2: apolipoprotein C-II
APOC3: apolipoprotein C-III
APOA5: apolipoprotein C-VI
ASO: antisense oligonucleotide
FCS: familial chylomicronemia syndrome
FDA: Food and Drug Administration
GPIHBP1: glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1
LMF1: lipase maturation factor 1
LPL: lipoprotein lipase

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of serious hypersensitivity reactions to olezarsen or any of the excipients in Tryngolza
- Boxed warning(s): none reported

Appendix D: General Information

- FCS may also be referred to as lipoprotein lipase deficiency (LPLD), type 1 hyperlipoproteinemia, endogenous hypertriglyceridemia, familial fat-induced hypertriglyceridemia, familial hyperchylomicronemia, familial LPL deficiency, hyperlipidemia Type I (Fredrickson), hyperlipoproteinemia type IA, lipase D deficiency, chylomicronemia syndrome, familial chylomicronemia, hyperchylomicronemia familial, hyperlipemia idiopathic Burger-Grutz type, lipase D deficiency, or Burger-Grutz syndrome.
- FCS is caused by biallelic loss-of-function homozygous, compound heterozygous, or double heterozygous pathogenic variants in LPL, APOC2, APOA5, GPIHBP1, and/or LMF1.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
FCS	80 mg SC once monthly	80 mg/month

VI. Product Availability

Single-dose autoinjector: 80 mg/0.8 mL

VII. References

1. Tryngolza Prescribing Information. Carlsbad, CA: Ionis Pharmaceuticals Inc.; December 2024. Available at: https://tryngolza.com/. Accessed January 16, 2025.
2. Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al; Balance Investigators. Olezarsen, acute pancreatitis, and familial chylomicronemia syndrome. *N Engl J Med*. 2024 May 16;390(19):1781-1792. doi: 10.1056/NEJMoa2400201.
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 Aug;275:265-272. doi: 10.1016/j.atherosclerosis.2018.06.814.
4. Handelsman Y, Jellinger PS, Guerin CK, 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 Oct;26(10):1196-1224. doi: 10.4158/CS-2020-0490.
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. *Circulation.* 2019 Jun 18;139(25):e1082-e1143. doi: 10.1161/CIR.0000000000000625.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date
Policy created	02/2025