Clinical Policy: Olezarsen (Tryngolza)

Reference Number: CP.PHAR.689
Effective Date: 12.18.24
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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;
4. Dose does not exceed 80 mg per month.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

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.; January 2025. Available at: www.tryngolza.com. Accessed May 8, 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	P&T Approval Date
Policy created pre-emptively	07.16.24	08.24
Drug is now FDA approved – criteria updated per FDA labeling; consolidated FCS diagnostic criteria; removed requirement for specific type of loss-of-function mutation from genetic testing requirement; added diagnostic information in Appendix D; removed failure of fibrates and omega-3 fatty acids; references reviewed and updated.	01.16.25	
3Q 2025 annual review: no significant changes; references reviewed and updated.	05.08.25	08.25

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical

practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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