

Medical Drug Clinical Criteria

Subject: Tryngolza (olezarsen)

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Overview

This document addresses the use of Tryngolza (olezarsen), an antisense oligonucleotide targeting *APOC3* mRNA that is approved by the Food and Drug Administration (FDA) as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). Tryngolza is administered via subcutaneous injection once monthly.

Familial chylomicronemia syndrome (FCS) is a rare genetic disorder caused by a pathogenic mutation in the lipoprotein lipase (LPL) gene or one of its cofactors [apolipoprotein C-II (APOC2), apolipoprotein A-V (APOA5), high-density lipoprotein binding protein 1 (GP1HBP1), lipase maturation factor 1 (LMF1)]. Deficiency in LPL activity impairs catabolism of triglyceride-rich lipoproteins like chylomicrons. This leads to very severe hypertriglyceridemia that is associated with recurrent episodes of pancreatitis. Current treatment includes limiting dietary fat to less than or equal to 20 grams per day. Drugs approved for lowering triglycerides are generally ineffective in individuals with FCS.

The clinical efficacy of Tryngolza was assessed in a randomized, double-blind, placebo-controlled trial in 66 adults with genetically identified familial chylomicronemia syndrome. Inclusion parameters required a fasting triglyceride level greater than or equal to 880 mg/dL and a willingness to adhere to a diet consisting of less than or equal to 20 grams of fat per day. 71% of study participants had a history of acute pancreatitis within the previous 10 years. The primary end point was percent change in fasting triglyceride level at 6 months and favored the 80 mg Tryngolza dose compared to placebo.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Tryngolza (olezarsen)

Initial requests for Tryngolza (olezarsen) may be approved if the following criteria are met:

- I. Individual is 18 years of age or older; **AND**
- II. Individual has a diagnosis of familial chylomicronemia syndrome; **AND**
- III. Documentation is provided that diagnosis has been demonstrated by a pathogenic gene mutation in *LPL*, *APOC2*, *APOA5*, *GPIHBP1* or *LMF1* (Stroes 2024); **AND**
- IV. Documentation is provided that individual has a fasting triglyceride level greater than or equal to 500 mg/dL (Grundy 2018); **AND**
- V. Individual will be using Tryngolza (olezarsen) in combination with a very low-fat diet (less than 20 gm per day of fat).

Continuation requests for Tryngolza (olezarsen) may be approved if the following criteria are met:

- I. Individual has a diagnosis of familial chylomicronemia syndrome; **AND**
- II. Documentation is provided that diagnosis has been demonstrated by a pathogenic gene mutation in *LPL*, *APOC2*, *APOA5*, *GPIHBP1* or *LMF1* (Stroes 2024); **AND**

- III. Documentation is provided that there is a clinically significant reduction in fasting triglyceride level with Tryngolza (olezarsen) therapy; **AND**
- IV. Individual is using Tryngolza (olezarsen) in combination with a very low-fat diet (less than 20 gm per day of fat).

Approval Duration
 Initial: 6 months
 Continuation: 1 year

Quantity Limits

Tryngolza (olezarsen) Quantity Limit

Drug	Limit
Tryngolza (olezarsen) 80 mg/0.8 mL	1 autoinjector per month

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

- C9399 Unclassified drugs or biologicals [when specified as Tryngolza (olezarsen)]
- J3490 Unclassified drugs [when specified as Tryngolza (olezarsen)]

ICD-10 Diagnosis

All diagnosis pend

Document History

New: 1/8/2025

Document History:

- 1/8/2025 – Select Review: New clinical criteria and quantity limit for Tryngolza. Administrative update to add documentation. Coding Reviewed: Added HCPCS NOC C9399, J3490, and all diagnosis pend.

References

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