Tryngolza®
(olezarsen) injection

Clinical FAQs

Evidence-based guidance for adults with severe hypertriglyceridemia (sHTG; TGs ≥500 mg/dL)

TRYNGOLZA is indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS) and to reduce triglycerides and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG).[1]

TG=triglyceride.

INDICATIONS

Familial Chylomicronemia Syndrome (FCS)

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

Severe Hypertriglyceridemia (sHTG)

TRYNGOLZA is indicated as an adjunct to diet to reduce TG and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG: TG ≥500 mg/dL).

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TRYNGOLZA is contraindicated in patients with a history of serious hypersensitivity to TRYNGOLZA or any of the excipients in TRYNGOLZA. Hypersensitivity reactions requiring medical treatment have occurred.

Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA, also available at TRYNGOLZAHCP.com.

Reference: 1. TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals.

Clinical answers to common questions

Adults with sHTG (TGs ≥500 mg/dL) face an elevated risk of acute pancreatitis (AP), and many remain above 500 mg/dL despite diet and background lipid-lowering therapy.[1-3]

TRYNGOLZA is the first and only FDA-approved therapy to reduce triglycerides and the risk of acute pancreatitis in adults with sHTG, as an adjunct to diet.[4] It gives you a new way to target apolipoprotein C-III (apoC-III), a key regulator of triglyceride metabolism, at its source in the liver.[4-6]

About this resource

This guide provides evidence-based answers to common clinical questions about TRYNGOLZA for adults with sHTG, organized into 4 sections:

Clinical foundation:
indication, mechanism of action, and pivotal trial design

Clinical evidence:
efficacy data including triglyceride lowering and acute pancreatitis, monitoring guidance, and safety profile

Dosing and administration:
flexible dosing options and autoinjector use

Access and support:
prescribing workflow, affordability programs, and Ionis Every Step™ patient services

How to use this guide

Use the Table of Contents to navigate to a specific question. All clinical answers are grounded in data from the CORE and CORE2 phase 3 trials.

TG=triglyceride.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (including symptoms of bronchospasm, diffuse erythema, facial swelling, urticaria, chills, and myalgias) have been reported in patients treated with TRYNGOLZA. Advise patients on the signs and symptoms of hypersensitivity reactions and instruct patients to promptly seek medical attention and discontinue use of TRYNGOLZA if hypersensitivity reactions occur.

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References: 1. Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of dyslipidemia: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2026:S0735-1097(25)10254-4. **2.** Marston NA, Bergmark BA, Alexander VJ, et al. Olezarsen for managing severe hypertriglyceridemia and pancreatitis risk. *N Engl J Med*. 2026;394(5):429-441. **3.** Skulas-Ray AC, Wilson PWF, Harris WS, et al. Omega-3 fatty acids for the management of hypertriglyceridemia: a science advisory from the American Heart Association. *Circulatio*n. 2019;140(12):e673-e691. **4.** TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals. **5.** Brinton EA, Eckel RH, Gaudet D, et al. Familial chylomicronemia syndrome and treatments to target hepatic APOC3 mRNA. *Atherosclerosis*. 2025;403:119114. **6.** Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al; Balance Investigators. Olezarsen, acute pancreatitis, and familial chylomicronemia syndrome. *N Engl J Med*. 2024;390(19):1781-1792.

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Clinical Foundation

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Q1.

What is TRYNGOLZA and what are the indications?

TRYNGOLZA is a GalNAc-conjugated antisense oligonucleotide indicated as an adjunct to diet to reduce triglycerides (TGs) and the risk of acute pancreatitis in adults with sHTG (TGs ≥500 mg/dL) and to reduce TGs in adults with FCS.[1]

Severe hypertriglyceridemia (sHTG) puts millions of American adults at risk of potentially life-threatening acute pancreatitis and is a risk-enhancing factor for atherosclerotic cardiovascular disease.[2-7] TRYNGOLZA is the first and only FDA-approved therapy to reduce TGs and the risk of acute pancreatitis for adults with sHTG as an adjunct to diet.[1]

TRYNGOLZA treats both sHTG and FCS through a proven mechanism of action that targets apolipoprotein C-III at its source in the liver.[1,8,9]

GalNAc=N-acetylgalactosamine.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Adverse Reactions for FCS

Most common adverse reactions in patients with FCS (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count, and arthralgia.

Adverse Reactions for sHTG

Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

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References: 1. TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals. **2.** Christian JB, Bourgeois N, Snipes R, Lowe KA. Prevalence of severe (500 to 2,000 mg/dl) hypertriglyceridemia in United States adults. *Am J Cardiol*. 2011;107(6):891-897. **3.** Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of dyslipidemia: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2026:S0735-1097(25)10254-4. **4.** Nawaz H, Koutroumpakis E, Easler J, et al. Elevated serum triglycerides are independently associated with persistent organ failure in acute pancreatitis. *Am J Gastroenterol*. 2015;110(10):1497-1503. **5.** Arca M, Veronesi C, D'Erasmo L, et al. Association of hypertriglyceridemia with all-cause mortality and atherosclerotic cardiovascular events in a low-risk Italian population: the TG-REAL retrospective cohort analysis. *J Am Heart Assoc*. 2020;9(19):e015801. **6.** Gurevitz C, Chen L, Muntner P, Rosenson RS. Hypertriglyceridemia and multiorgan disease among U.S. adults. *JACC Adv*. 2024;3(5):100932. **7.** Ginsberg HN, Packard CJ, Chapman MJ, et al. Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies—a consensus statement from the European Atherosclerosis Society. *Eur Heart J*. 2021;42(47):4791-4806. **8.** Brinton EA, Eckel RH, Gaudet D, et al. Familial chylomicronemia syndrome and treatments to target hepatic APOC3 mRNA. *Atherosclerosis*. 2025;403:119114. **9.** Stroes ESG, Alexander VJ, Karwatowska-Prokopczuk E, et al; Balance Investigators. Olezarsen, acute pancreatitis, and familial chylomicronemia syndrome. *N Engl J Med*. 2024;390(19):1781-1792.

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Q2.

How does TRYNGOLZA work?

TRYNGOLZA enables targeted delivery to the liver, where apoC-III messenger RNA (mRNA) is generated.[1-3]

ApoC-III is a pivotal regulator of triglyceride metabolism across the sHTG spectrum, inhibiting lipoprotein lipase activity and impairing hepatic clearance of triglyceride-rich lipoproteins.[1-3] By targeting apoC-III at its source, TRYNGOLZA addresses a foundational driver of elevated triglycerides.[1-3]

The mechanism involves 3 steps:

1. Targeting hepatocytes: GalNAc enables targeted delivery to the liver[1,2]
2. Selectively binding to apoC-III mRNA: In the hepatocyte, TRYNGOLZA directly and selectively binds to apoC-III mRNA[1,3]
3. Degrading apoC-III mRNA: TRYNGOLZA induces RNase cleavage of apoC-III mRNA, leading to its degradation[1-3]

This mechanism leads to reduced serum apoC-III and increased clearance of plasma triglycerides, very low-density lipoprotein, and chylomicrons.[1,3]

apoC-III=apolipoprotein C-III; GalNAc=N-acetylgalactosamine.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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Q3.

How was TRYNGOLZA studied in patients with sHTG?

TRYNGOLZA was evaluated in CORE and CORE2,* 2 randomized, double-blind, placebo-controlled, phase 3 studies that included a total of 1061 adults with sHTG.[1,2]

In both studies, adult patients with sHTG (N=1061) were randomized to receive TRYNGOLZA 50 mg, TRYNGOLZA 80 mg, or placebo once every 4 weeks for a 53-week treatment period.[1] More than 90% of patients who completed treatment rolled over to the sHTG open-label extension.[3]

*Trial 2 and Trial 3 in the full Prescribing Information.[1]

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (including symptoms of bronchospasm, diffuse erythema, facial swelling, urticaria, chills, and myalgias) have been reported in patients treated with TRYNGOLZA. Advise patients on the signs and symptoms of hypersensitivity reactions and instruct patients to promptly seek medical attention and discontinue use of TRYNGOLZA if hypersensitivity reactions occur.

Liver Enzyme Abnormalities

TRYNGOLZA can cause increases in liver enzymes and hepatic fat in adults. Increases in liver enzymes were more frequently reported with the 80 mg dose as compared with the 50 mg dose. Consider liver enzyme testing before TRYNGOLZA initiation or an increase in dosage and when clinically indicated thereafter. If persistent elevations in liver enzymes occur, consider dose interruption and/or dose reduction. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue TRYNGOLZA.

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Q4.

How much does TRYNGOLZA lower triglycerides?

Up to 72% statistically significant mean change in fasting TGs with TRYNGOLZA 80 mg compared with placebo at Month 6* (*P*<0.0001).[1]

In CORE, TRYNGOLZA 50 mg and 80 mg demonstrated a statistically significant mean change of -63% and -72%, respectively, in fasting triglycerides from baseline to Month 6* compared with placebo (*P*<0.0001)[1]

In CORE2, TRYNGOLZA 50 mg and 80 mg demonstrated a statistically significant mean change of -49% and -55%, respectively, in fasting triglycerides from baseline to Month 6* compared with placebo (*P*<0.0001)[1]

Triglyceride reduction from baseline at Month 6 was 63% in both studies with TRYNGOLZA 50 mg and 73% and 68% with TRYNGOLZA 80 mg in CORE and CORE2, respectively. Monthly dosing provided consistent TG lowering throughout the 12-month treatment period.[1]

*Average of Weeks 25 and 27.[1]
TG=triglyceride.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Adverse Reactions for FCS

Most common adverse reactions in patients with FCS (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count, and arthralgia.

Adverse Reactions for sHTG

Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

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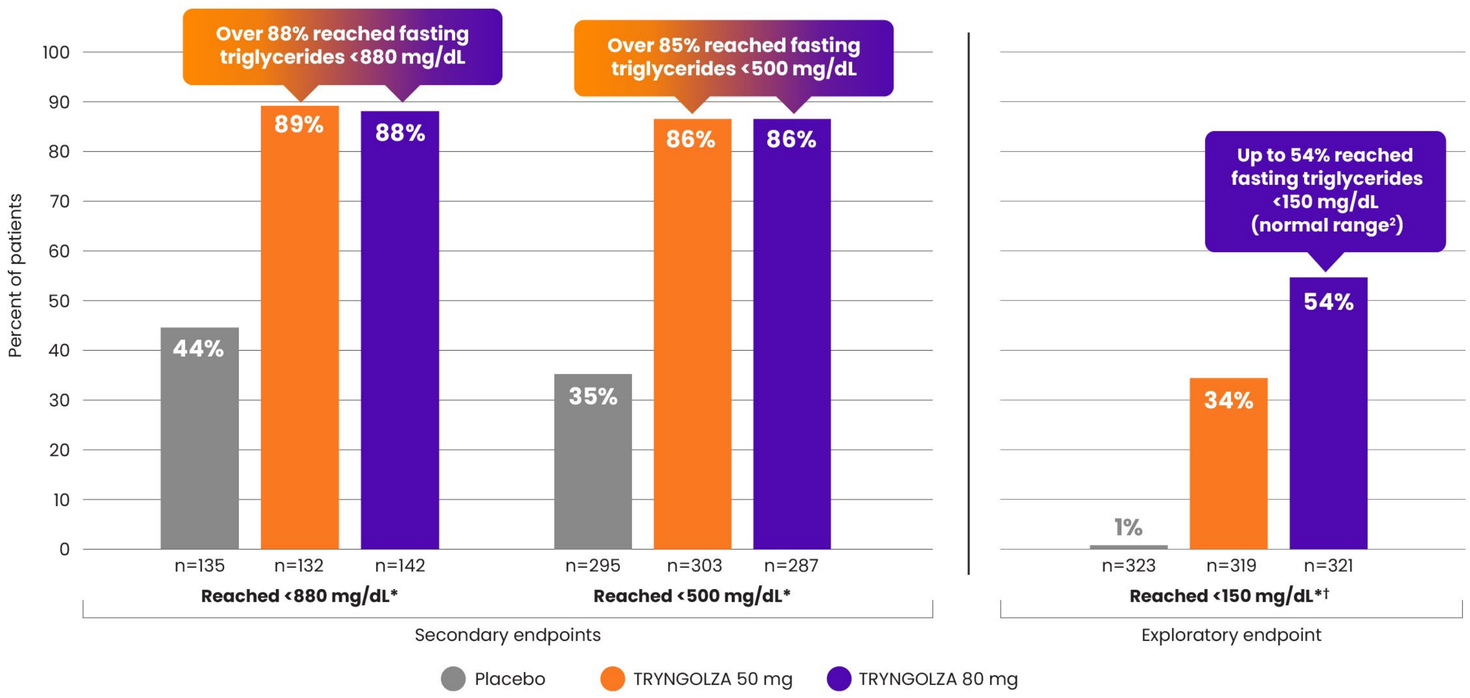
Q5.

Does TRYNGOLZA get patients with sHTG below 500 mg/dL or even below 150 mg/dL?

Yes, triglyceride levels <880 mg/dL, <500 mg/dL, and <150 mg/dL were observed at 12 months. More than 85% of patients reached triglyceride levels <500 mg/dL with TRYNGOLZA.[1]

In pooled responder analyses at 1 year[1]:



†**LIMITATION:**
Data shown were exploratory analyses; observed results should be interpreted with caution.

*Achievement of triglyceride levels ‹880 mg/dL, <500 mg/dL, and <150 mg/dL at 12 months among patients with baseline levels above these thresholds.[1]

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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Q6.

Does TRYNGOLZA reduce the risk of acute pancreatitis?

Yes. TRYNGOLZA is the first and only therapy indicated as an adjunct to diet to reduce triglycerides and the risk of acute pancreatitis (AP) in adults with sHTG.[1]

In an integrated analysis of CORE and CORE2 (N=1061), TRYNGOLZA 50 mg achieved up to a 91% reduction in the adjudicated AP event rate compared with placebo, in addition to background lipid-lowering therapy (RR: 0.09; 95% CI: 0.02, 0.42).[1]

AP event rate reduction by dose compared with placebo[1]:

- TRYNGOLZA 50 mg: -91% (RR: 0.09; 95% CI: 0.02, 0.42)
- TRYNGOLZA 80 mg: -76% (RR: 0.24; 95% CI: 0.08, 0.69)

Across the combined pooled TRYNGOLZA group, there was an 85% reduction in the adjudicated AP event rate from baseline to 1 year vs placebo (RR: 0.15; 95% CI: 0.05, 0.40).[1]

- 17 patients (4.8%) in the pooled placebo group experienced 22 events of adjudicated AP[1]
- 5 patients (0.7%) in the combined pooled TRYNGOLZA group experienced 7 events[1]

TRYNGOLZA also demonstrated a statistically significant longer time to first acute pancreatitis event vs placebo (log-rank $P<0.0001$).[1]

Pancreatitis events were assessed as a secondary endpoint in an integrated analysis of CORE and CORE2. Events were adjudicated by a blinded, independent committee according to the Revised Atlanta Diagnostic Criteria. Event rates over 53 weeks were compared between pooled TRYNGOLZA (50 mg and 80 mg) and pooled placebo using a negative binomial regression model.[1]

The time was censored at Week 53 or at the posttreatment follow-up termination date, whichever occurred first. The time to the first adjudicated pancreatitis event was compared between the pooled TRYNGOLZA treatment group and the placebo group using a log-rank test, stratified by study identifier (CORE or CORE2).[1]

RR=rate ratio.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

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Q7.

How does TRYNGOLZA differ from other TG-lowering therapies?

TRYNGOLZA is the first and only FDA-approved therapy to reduce triglycerides and the risk of acute pancreatitis in adults with sHTG, as an adjunct to diet, injected subcutaneously once monthly via a convenient autoinjector.[1,2]

Standard-of-care treatments (omega-3 fatty acids, fibrates, statins) can help lower triglycerides, but their ability to lower TGs in patients with sHTG can be inadequate, and none have been specifically studied to reduce acute pancreatitis events.[3-6] Most patients in CORE and CORE2 were already on background lipid-lowering therapy (42% high-intensity statins; 27% moderate-intensity statins; 63% fibrates; 32% omega-3 fatty acids) and still had severely elevated TGs at baseline (mean [SD] fasting TGs 1116 [990] mg/dL).[1]

TRYNGOLZA offers:

- An RNA-targeted mechanism that targets apoC-III at the source of production in the liver[1,7,8]
- Up to 72% placebo-corrected reduction in TGs at Month 6* (primary endpoint in CORE with 80 mg; *P*<0.0001), in addition to background lipid-lowering therapy[1]
  - In CORE, TRYNGOLZA 50 mg and 80 mg demonstrated a statistically significant mean change of -63% and -72%, respectively, in fasting TGs from baseline to Month 6* compared with placebo (*P*<0.0001)
  - In CORE2, TRYNGOLZA 50 mg and 80 mg demonstrated a statistically significant mean change of -49% and -55%, respectively, in fasting TGs from baseline to Month 6* compared with placebo (*P*<0.0001)
- Up to 91% reduction in the adjudicated acute pancreatitis event rate with TRYNGOLZA 50 mg compared with placebo, in addition to background lipid-lowering therapy (RR: 0.09; 95% CI: 0.02, 0.42)[1]
  - 85% reduction in the adjudicated acute pancreatitis event rate with the combined pooled TRYNGOLZA group compared with placebo at Month 12 (RR: 0.15; 95% CI: 0.05, 0.40)[1]
- A well-tolerated safety profile in participants with sHTG. Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases[1]
- Once-monthly self-administration via a convenient autoinjector with flexible dosing (see Q14 for dosing information)[1,2]

TRYNGOLZA can help address a persistent treatment gap for patients whose TGs remain elevated despite conventional approaches.[1,3]

*Average of Weeks 25 and 27.[1]
RR=rate ratio; SD=standard deviation; TG=triglyceride.

SELECT IMPORTANT SAFETY INFORMATION
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Adverse Reactions for FCS
Most common adverse reactions in patients with FCS (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count, and arthralgia.

Adverse Reactions for sHTG
Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

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Q8.

How quickly does TRYNGOLZA start working?

TRYNGOLZA delivers rapid triglyceride (TG) reduction with consistent control over 1 year. TG reductions were observed by Week 5, the first post-baseline measurement, and were consistent through 12 months of treatment.[1]

Up to 72% placebo-corrected reduction in TGs at Month 6* (primary endpoint in CORE with 80 mg; *P*<0.0001), in addition to background lipid-lowering therapy:

In CORE, TRYNGOLZA 50 mg and 80 mg demonstrated a statistically significant mean change of -63% and -72%, respectively, in fasting triglycerides from baseline to Month 6* compared with placebo (*P*<0.0001)[1]

In CORE2, TRYNGOLZA 50 mg and 80 mg demonstrated a statistically significant mean change of -49% and -55%, respectively, in fasting triglycerides from baseline to Month 6* compared with placebo (*P*<0.0001)[1]

Monthly dosing with TRYNGOLZA provided consistent TG lowering throughout the 12-month treatment period.[1]

*Average of Weeks 25 and 27.[1]

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CONTRAINDICATIONS

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Q9.

How often should triglyceride levels be monitored in patients taking TRYNGOLZA?

No specific triglyceride (TG) monitoring is required in the Prescribing Information.

Assess TGs when clinically appropriate. The TG-lowering effect of TRYNGOLZA may be measured within 3 months after initiation.[1]

In the CORE and CORE2 clinical trials, rapid TG reductions were observed as early as Week 5, the first post-baseline measurement, and were consistent through 12 months of treatment, with the primary endpoint evaluated at Month 6.[1*]

The 2026 ACC/AHA Guideline on the Management of Dyslipidemia recommends performing a lipid profile 1 to 3 months after initiation or dose adjustment of lipid-lowering therapy and then every 6 to 12 months thereafter to assess efficacy and adherence.[2]

TG monitoring is at the discretion of the healthcare provider based on individual patient needs.

*Average of Weeks 25 and 27.[1]
ACC=American College of Cardiology; AHA=American Heart Association.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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TRYNGOLZA can cause increases in liver enzymes and hepatic fat in adults. Increases in liver enzymes were more frequently reported with the 80 mg dose as compared with the 50 mg dose. Consider liver enzyme testing before TRYNGOLZA initiation or an increase in dosage and when clinically indicated thereafter. If persistent elevations in liver enzymes occur, consider dose interruption and/or dose reduction. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue TRYNGOLZA.

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Q10.

What are the most common adverse events with TRYNGOLZA?

The most common adverse reactions (≥2% higher frequency vs placebo) in patients with sHTG were injection-site reactions and liver enzyme increases.[1]

The majority of injection-site reactions were mild and none were severe.[2]

Injection-site reactions:
12% (50 mg) and 18% (80 mg) vs 2% (placebo).[1] The majority were mild and none were severe.[2]

Transaminases increased:
3% (50 mg) and 4% (80 mg) vs 1% (placebo). Mean liver enzyme values increased from baseline with TRYNGOLZA treatment but remained within the normal range.[1]

TRYNGOLZA demonstrated a well-tolerated safety profile in CORE and CORE2 (n=705 pooled TRYNGOLZA; n=356 pooled placebo). Adverse reactions led to discontinuation in 5% of TRYNGOLZA-treated patients vs 2% of placebo-treated patients; the most common adverse reaction leading to TRYNGOLZA treatment discontinuation was injection-site reactions.[1]

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Adverse Reactions for FCS

Most common adverse reactions in patients with FCS (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count, and arthralgia.

Adverse Reactions for sHTG

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Q11.

What monitoring is recommended for patients taking TRYNGOLZA?

No specific monitoring is required in the Prescribing Information.

Consider liver enzyme testing before TRYNGOLZA initiation or an increase in dosage and when clinically indicated thereafter. If persistent elevations in liver enzymes occur (such as 3 times the upper limit of normal or greater), consider dose interruption and/or dose reduction. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue TRYNGOLZA.[1]

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TRYNGOLZA is contraindicated in patients with a history of serious hypersensitivity to TRYNGOLZA or any of the excipients in TRYNGOLZA. Hypersensitivity reactions requiring medical treatment have occurred.

Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA, also available at TRYNGOLZAHCP.com.

Reference: 1. TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals.

Tryngolza®
(olezarsen) injection

Q12.

Can I use TRYNGOLZA in sHTG patients with poorly controlled diabetes?

Yes. Adults with sHTG and diabetes were eligible for the CORE and CORE2 trials. In the trials, 63% of patients had type 2 diabetes mellitus.[1,2]

In the overall trial population, small increases in fasting glucose (≤9 mg/dL) and HbA1c (<0.3 percentage points) were observed with TRYNGOLZA, predominantly in patients with a history of diabetes.[2]

Patients with HbA1c ≥9.5% at screening were excluded.[1]

TRYNGOLZA was studied on top of background lipid-lowering therapy and can be used alongside a patient's existing diabetes regimen.[2]

HbA1c=hemoglobin A1c.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (including symptoms of bronchospasm, diffuse erythema, facial swelling, urticaria, chills, and myalgias) have been reported in patients treated with TRYNGOLZA. Advise patients on the signs and symptoms of hypersensitivity reactions and instruct patients to promptly seek medical attention and discontinue use of TRYNGOLZA if hypersensitivity reactions occur.

Liver Enzyme Abnormalities

TRYNGOLZA can cause increases in liver enzymes and hepatic fat in adults. Increases in liver enzymes were more frequently reported with the 80 mg dose as compared with the 50 mg dose. Consider liver enzyme testing before TRYNGOLZA initiation or an increase in dosage and when clinically indicated thereafter. If persistent elevations in liver enzymes occur, consider dose interruption and/or dose reduction. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue TRYNGOLZA.

Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA, also available at TRYNGOLZAHCP.com.

References: 1. Marston NA, Bergmark BA, Alexander VJ, et al. Olezarsen for managing severe hypertriglyceridemia and pancreatitis risk. *N Engl J Med*. 2026;394(5):429-441.
2. TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals.

Tryngolza®
(olezarsen) injection

Q13.

Can TRYNGOLZA be used alongside GLP-1 receptor agonists?

Patients receiving background metabolic therapies, including GLP-1 receptor agonists, were included in the CORE and CORE2 clinical program. In CORE and CORE2, 15.9% of patients and 16.9% of patients, respectively, were concomitantly receiving GLP-1s in the trials.[1,2] In CORE and CORE2, TRYNGOLZA was studied in patients with diabetes who were receiving background diabetes therapy in addition to optimized, stable background lipid-lowering therapy.[3]

Physicians should continue standard clinical management appropriate for the patient's underlying metabolic conditions and concomitant therapies.

GLP-1=glucagon-like peptide-1.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Adverse Reactions for FCS

Most common adverse reactions in patients with FCS (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count, and arthralgia.

Adverse Reactions for sHTG

Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA, also available at TRYNGOLZAHCP.com.

References: 1. Data on file. REF-03800. Ionis Pharmaceuticals; 2025. **2.** Data on file. REF-03801. Ionis Pharmaceuticals; 2025. **3.** TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals.

Tryngolza® (olezarsen) injection

Q14.

How is TRYNGOLZA dosed?

TRYNGOLZA is a once-monthly subcutaneous injection used as an adjunct to diet.[1]

In adults with sHTG[1]:

- The recommended dosage of TRYNGOLZA is **50 mg** injected subcutaneously once monthly with a low-fat diet
- Assess triglycerides (TGs) when clinically appropriate. The TG-lowering effect of TRYNGOLZA may be measured within 3 months after initiation
- For patients who tolerate the **50 mg** dosage and additional TG reduction is clinically indicated, the dosage may be increased to **80 mg** injected subcutaneously once monthly

In adults with FCS[1]:

- The recommended dosage of TRYNGOLZA is **80 mg** once monthly with a low-fat diet of ≤20 grams fat per day

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Reference: 1. TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals.

Tryngolza® (olezarsen) injection

Q15.

How is TRYNGOLZA administered?

TRYNGOLZA is self-administered via a convenient autoinjector.[1,2]

The 3-step (place, push, hold) convenient autoinjector is designed for ease of use, and the once-monthly schedule supports clinical choice based on individual patient needs.[1,2] The autoinjector can be stored at room temperature for up to 6 weeks, allowing patients to administer their dose at home or away from home.[1]

The autoinjector should be stored in the refrigerator between 36 °F and 46 °F (2-8 °C) in the original carton; it can be stored at room temperature between 59 °F and 86 °F (15-30 °C) for up to 6 weeks.[1]*

For full details on administration and storage, see the Instructions for Use and the injection training video at TRYNGOLZAHCP.com.

*If not used within the 6 weeks stored at room temperature, discard TRYNGOLZA.[1]

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WARNINGS AND PRECAUTIONS

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Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA, also available at TRYNGOLZAHCP.com.

References: 1. TRYNGOLZA. Prescribing information. Ionis Pharmaceuticals. **2.** Data on file. REF-01291. Ionis Pharmaceuticals; 2024.

Tryngolza® (olezarsen) injection

Q16.

Can TRYNGOLZA be used with other lipid-lowering therapies?

In the CORE and CORE2 trials, 99% of patients were on background lipid-lowering therapies, and TRYNGOLZA demonstrated significant triglyceride reductions on top of these existing therapies.[1]

Background therapies included statins (42% high-intensity; 27% moderate-intensity), fibrates (63%), and omega-3 fatty acids (32%).[1]

- Patients were on optimized, stable background lipid-lowering therapy prior to enrollment and throughout the study

TRYNGOLZA 50 mg and 80 mg demonstrated a significant mean change of -63% and -72% in CORE and -49% and -55% in CORE2, respectively, in fasting triglycerides from baseline to Month 6* compared with placebo ($P<0.0001$; primary endpoint).[1]

TRYNGOLZA is indicated as an adjunct to diet and can be added to a patient's current lipid-lowering regimen.[1]

*Average of Weeks 25 and 27.[1]

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ADVERSE REACTIONS

Adverse Reactions for FCS

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Adverse Reactions for sHTG

Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

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Tryngolza®
(olezarsen) injection

Q17.

What should I expect when prescribing TRYNGOLZA?

Prescribing TRYNGOLZA is designed to minimize administrative burden on your office. After you prescribe, an in-network specialty pharmacy partner manages benefits verification, prior authorization, and appeals, while Ionis Every Step™ supports your patient through approval, onboarding, and ongoing treatment.

Workflow at a glance:

Prescribe
Download the TRYNGOLZA Start Form at TRYNGOLZAHCP.com and fax to an in-network pharmacy, or e-prescribe through your electronic health record (EHR) system

Coverage support
In-network pharmacies handle benefits verification, prior authorizations and reauthorizations, and appeals

Patient onboarding
Confirm patient consent so Ionis Every Step can engage them directly

Affordability options for eligible patients

- $0 copay for commercially insured patients (Ionis Every Step Copay Program)*
- Quick Start: first dose at no cost if coverage is delayed
- Patient Assistance Program (PAP) for uninsured/underinsured patients†

*Eligibility restrictions apply. This program is not available to individuals who use any state or federal government-funded health care program to cover a portion of medication costs.
†Subject to program terms, conditions, and limits.

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Tryngolza®
(olezarsen) injection

Q18.

What support is available for patients taking TRYNGOLZA?

Ionis Every Step™ offers a broad range of support to help your patients at every step of their TRYNGOLZA treatment journey.

Beyond access and affordability, patients have access to ongoing support and education throughout their treatment.

Support to start and stay on treatment:
Ongoing support throughout treatment, such as injection training, regular check-ins, and connecting patients with an extra level of support, if needed

Patient education and engagement:
Continued access to digital resources keeping patients informed about how to manage their health and providing additional training on how to use TRYNGOLZA

Encourage your patients to enroll online at TRYNGOLZA.com/Enroll, or they can call the Ionis Every Step TRYNGOLZA Support Center at 1-844-789-8744 (select option 2), Monday to Friday, 8 AM to 8 PM ET.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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