Tryngolza®
(olezarsen) injection

In adults with severe hypertriglyceridemia (sHTG; TGs ≥500 mg/dL)[1]

HELP GET YOUR PATIENTS OUT OF THE DANGER ZONE

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.[1]

TG=triglyceride.

INDICATION

TRYNGOLZA (olezarsen) is indicated as an adjunct to diet to reduce triglycerides (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.

Severe hypertriglyceridemia (sHTG) puts millions of adults at risk of potentially life-threatening acute pancreatitis (AP) and atherosclerotic cardiovascular disease (ASCVD)[2-7]

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sHTG, defined as fasting triglyceride levels ≥500 mg/dL, includes metabolic and genetic forms such as familial chylomicronemia syndrome (FCS)[3,8]

The risk of AP increases at 500 mg/dL and becomes significantly more pronounced at fasting triglyceride levels of >880 mg/dL because of the accumulation of very low-density lipoprotein (VLDL) and chylomicrons at this level[3,7,9-11]

- Chylomicrons (marked by apolipoprotein B-48) and VLDL (marked by apolipoprotein B-100) contribute to AP risk[3,7]
- VLDL and their remnant cholesterol contribute to ASCVD[3,7]

*In a study of 1.8 million adults, acute pancreatitis risk vs those with normal triglyceride levels (<150 mg/dL).[12]

sHTG-induced AP has serious consequences

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Even a single episode of AP can have significant consequences. Once a patient with sHTG has had an episode of AP, the **chance of another event is as high as 24%**, and the chance of **a third event after a second rises to 49%**[13*]

sHTG-induced AP can lead to:

Mortality rate as high as 8%[4,14]

Irreversible multisystem organ damage, including pancreatic necrosis[14,15]

Prolonged hospitalization of around 17 days per incident[4,14]

Beta-cell dysfunction leading to pancreatogenic diabetes (type 3c diabetes mellitus)[14,15]

Healthcare-related costs of around $100K per incident[16†]

- **Standard-of-care treatments**' ability to lower triglyceride levels in patients with sHTG can be inadequate, and **none have demonstrated efficacy in reducing risk of AP**[3,17,18]

*Retrospective claims database analysis of 7,119,195 US patients. Acute pancreatitis event risk was assessed based on the presence or absence of acute pancreatitis events within the previous 12 months.[13]
†In total costs for hospitalization and the 12 months following an AP event.[16]
AP=acute pancreatitis; sHTG=severe hypertriglyceridemia.

sHTG in the 2026 ACC/AHA/ADA dyslipidemia and cardiovascular-kidney-metabolic (CKM) syndrome guidelines

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<500 mg/dL

The 2026 ACC/AHA/ADA guidelines on dyslipidemia and CKM syndrome, along with the National Lipid Association and Endocrine Society guidelines, identify TGs <500 mg/dL as a critical threshold for reducing acute pancreatitis risk.[3,19-21]

TG RISK STRATIFICATION	CONFIRMING sHTG	ASCVD RISK ASSESSMENT	RESPONSE MONITORING
Risk varies by TG stratum[3] **CV risk** is highest at TGs 500-880 mg/dL. **AP risk** increases at ≥500 mg/dL; particularly high at ≥1000 mg/dL.	**Workup before treatment[3]** **Confirm fasting** TGs ≥500 mg/dL on repeat measurement. Identify secondary causes (uncontrolled diabetes, alcohol, obesity, etc).	**Beyond LDL-C: apoB and non–HDL-C[3]** **Non–HDL-C and apoB are considered more accurate estimators of ASCVD risk than LDL-C** in patients with hypertriglyceridemia.	**When to reassess TG levels[3]** Perform a lipid profile **1-3 months** after treatment initiation or dose adjustment, then **every 6-12 months** thereafter.

ACC=American College of Cardiology; ADA=American Diabetes Association; AHA=American Heart Association; apoB=apolipoprotein B; CV=cardiovascular; LDL-C=low-density lipoprotein cholesterol; non–HDL-C=non–high-density lipoprotein cholesterol.

A proven mechanism of action that lowers apolipoprotein C-III (apoC-III) at its source[1]

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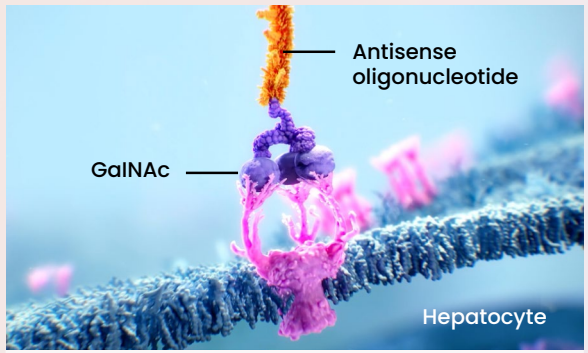
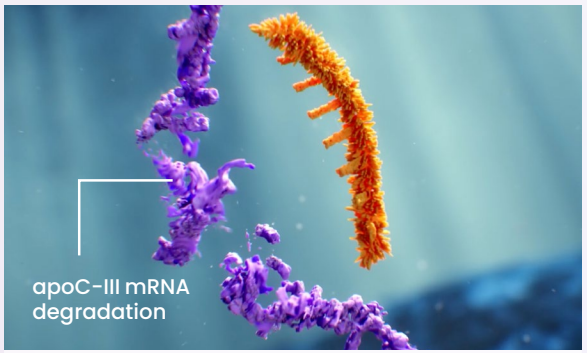
TRYNGOLZA is a GalNAc-conjugated antisense oligonucleotide that enables targeted delivery to the liver, where apoC-III, a key regulator of triglyceride metabolism, is generated[1,22,23]

TRYNGOLZA is designed to work by:



1 Targeting hepatocytes[1,22]

2 Selectively binding to apoC-III mRNA[1,23]



3 Degrading apoC-III mRNA[1,22,23]

This mechanism leads to reduced serum apoC-III and increased clearance of plasma triglycerides, VLDL, and chylomicrons.[1,23]

GalNAc=N-acetylgalactosamine; mRNA=messenger RNA; VLDL=very low-density lipoprotein.

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.

Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA.

CORE and CORE2* pivotal trial study designs

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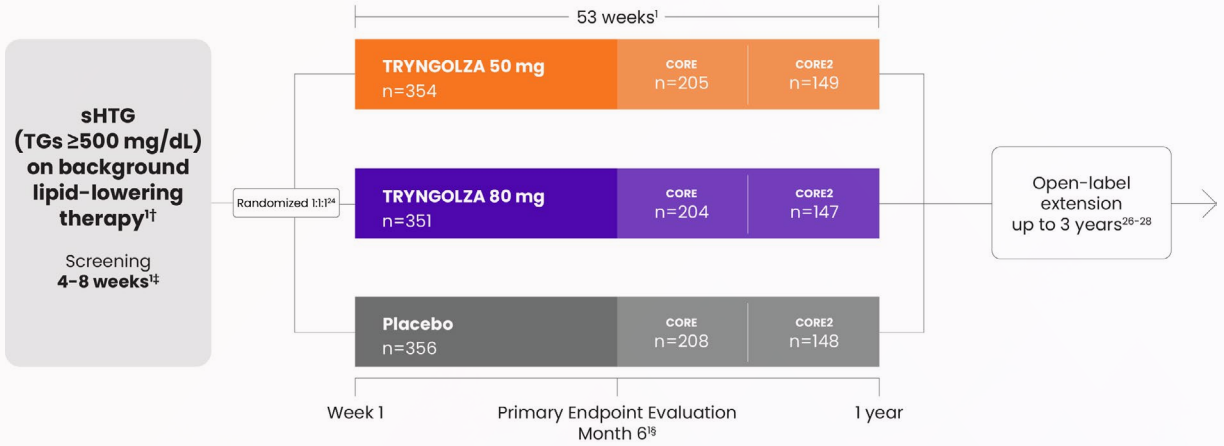
TRYNGOLZA was evaluated in 2 randomized, double-blind, placebo-controlled, phase 3 studies that included a total of 1061 adults with sHTG[1,24]

- 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]
- >90% of patients who completed treatment rolled over to the sHTG open-label extension (OLE)[25]
- Patients were eligible if they were ≥18 years of age, had sHTG (TGs ≥500 mg/dL), and were adherent to optimized stable background lipid-lowering therapy; key exclusion criteria were genetically confirmed FCS, recent AP, poorly controlled diabetes mellitus, and eGFR <30 mL per minute per 1.73 m^2 [1,24†]
- Participant demographics and baseline characteristics were generally similar across treatment groups in CORE and CORE2[1]



*Trial 2 and Trial 3 in the full Prescribing Information.[1]
†Background lipid-lowering therapy in CORE and CORE2 primarily included statins (42% high-intensity; 27% moderate-intensity), fibrates (63%), and omega-3 fatty acids (32%).[1]
‡Including at least 2 weeks of diet and lifestyle stabilization.[1]
§Average of Weeks 25 and 27.[1]
eGFR=estimated glomerular filtration rate; FCS=familial chylomicronemia syndrome.

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WARNINGS AND PRECAUTIONS

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.

Statistically significant, robust triglyceride reductions of up to 72% at 6 months in adults with sHTG[1]

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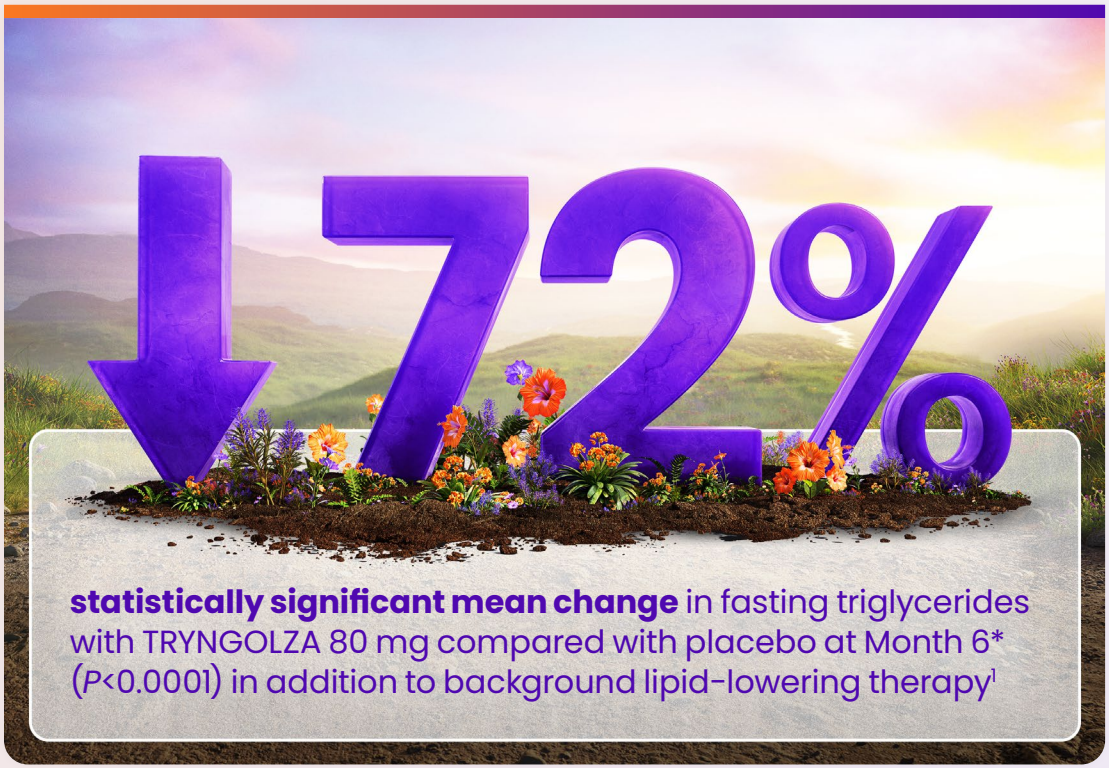
Primary endpoint

- Mean percent change in fasting triglyceride levels from baseline to Month 6* for both TRYNGOLZA 50 mg and 80 mg doses compared with placebo[1]



CORE[1]

TRYNGOLZA 50 mg	TRYNGOLZA 80 mg
1169 Mean baseline (mg/dL)	**1169** Mean baseline (mg/dL)
-63% **placebo-corrected** difference from baseline to Month 6*†	**-72%** **placebo-corrected** difference from baseline to Month 6*†

CORE2[1]

TRYNGOLZA 50 mg	TRYNGOLZA 80 mg
968 Mean baseline (mg/dL)	**1088** Mean baseline (mg/dL)
-49% **placebo-corrected** difference from baseline to Month 6*†	**-55%** **placebo-corrected** difference from baseline to Month 6*†

*Average of Weeks 25 and 27.[1]
†Reached statistical significance ($P<0.0001$).[1]

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

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.

Up to 91% reduction in acute pancreatitis events in adults with severe hypertriglyceridemia[1]

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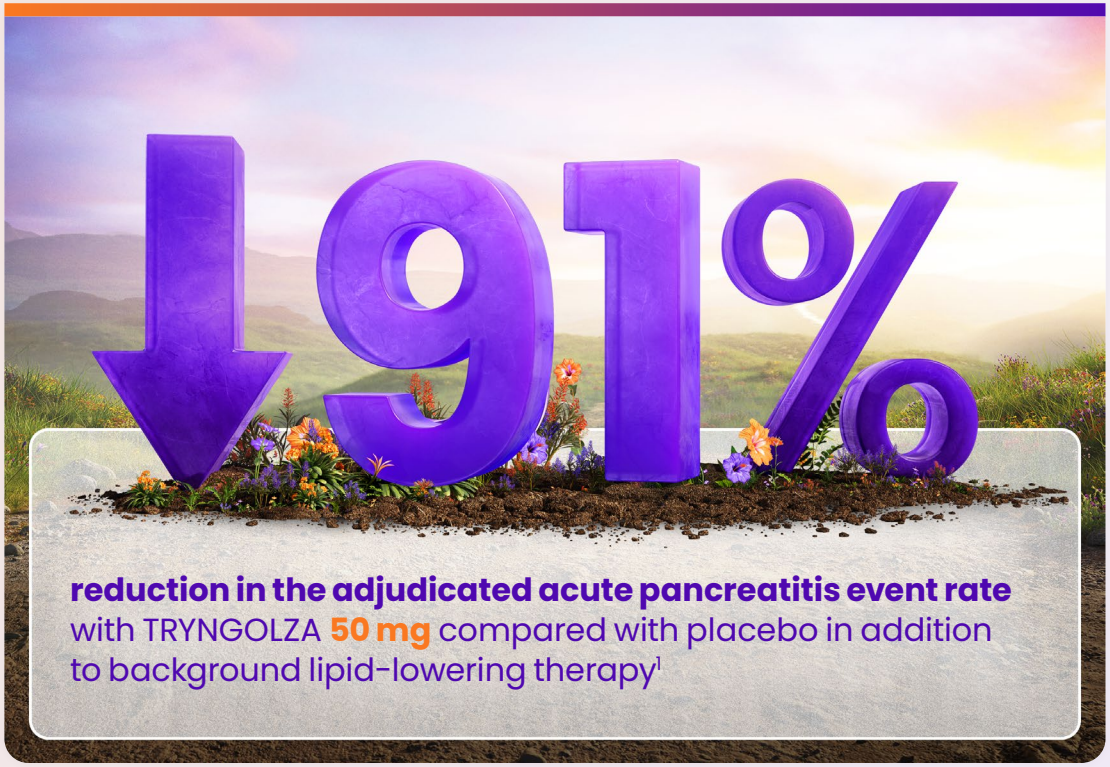

AP EVENT RATE REDUCTION BY DOSE COMPARED WITH PLACEBO[1]

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

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.[1]
RR=rate ratio.

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CONTRAINDICATIONS

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TRYNGOLZA is the first therapy indicated to reduce the risk of AP in adults with sHTG[1]

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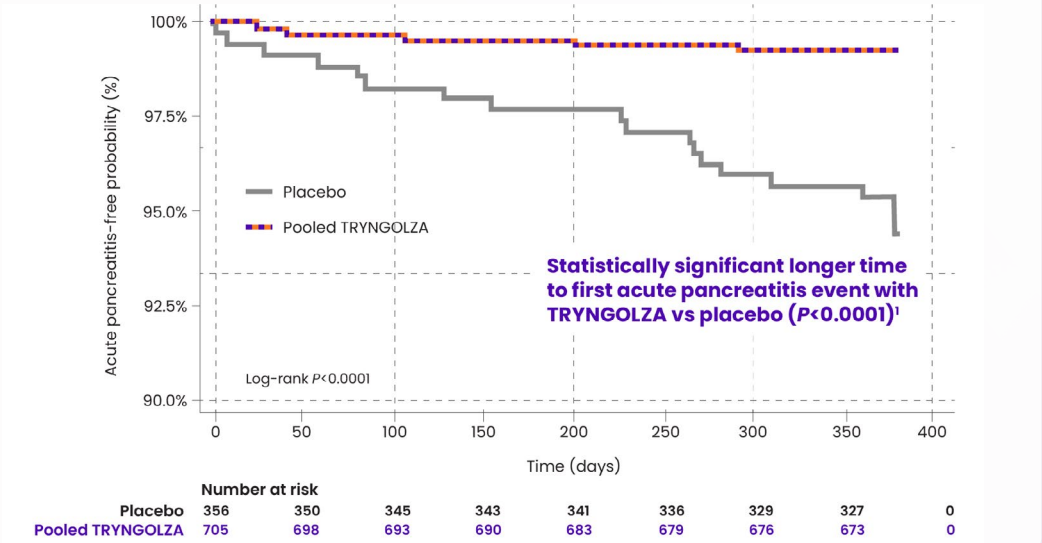
Kaplan-Meier estimate of time to first AP event in patients with sHTG (pooled analysis of CORE and CORE2) (N=1061)[1]



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]

85% reduction in AP events

(RR: 0.15; 95% CI: 0.05, 0.40) in the pooled TRYNGOLZA group[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]

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]

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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Low numbers needed to treat (NNT) were observed in patients most at risk of AP[12,24]

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- The NNT communicates how many patients on average would need to be on a given treatment for a defined period to benefit compared with not using the therapy[29,30]
- The lower the NNT, the more effective the treatment[30]

NNT with TRYNGOLZA over 1 year to prevent 1 AP event[24,31]

TGs ≥500 mg/dL	TGs ≥880 mg/dL	TGs ≥880 mg/dL + prior AP history
NNT=20*	**NNT=9***	**NNT=4***

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

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What is number needed to treat (NNT)?

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NNT is an important measure of efficacy

NNT RATINGS[32,33]	
NNT ≤6	Represents exceptional clinical benefit
NNT <20	Indicates strong clinical benefit
NNT 20–50	Considered acceptable therapeutic benefit depending on the severity of the condition being prevented
NNT >50	Generally represents marginal therapeutic benefit requiring careful consideration of treatment burden

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

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.

TRYNGOLZA demonstrated a well-tolerated safety profile in participants with sHTG[1]

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Adverse reactions* occurring in ≥2% of patients with sHTG treated with TRYNGOLZA than with placebo[1†]

	TRYNGOLZA 50 mg (n=354)	TRYNGOLZA 80 mg (n=351)	Placebo (n=356)
Injection-site reactions	43 (12%)	64 (18%)	8 (2%)
Transaminases increased	11 (3%)	14 (4%)	2 (1%)

- The safety of TRYNGOLZA was evaluated in 705 patients (50 mg pooled n=354; 80 mg pooled n=351) who received at least 1 dose of treatment and in 356 who received placebo[1]
- Adverse reactions led to discontinuation of treatment in 5% of TRYNGOLZA-treated patients and 2% of placebo-treated patients[1]
- The most common adverse reaction for TRYNGOLZA treatment discontinuation was injection-site reactions[1]

Most injection-site reactions were mild. None were severe.[24]

*Grouped terms composed of several similar terms.[1]
†Pooled analysis of CORE and CORE2.[1]

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CONTRAINDICATIONS

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Flexible, once-monthly dosing with TRYNGOLZA supports clinical choice based on individual patient needs[1]

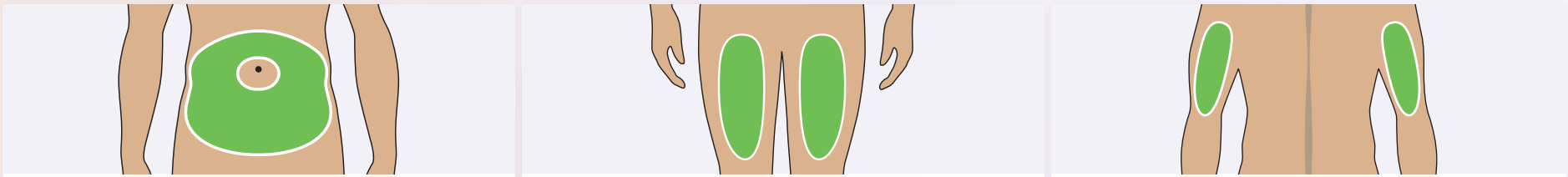
Tryngolza® (olezarsen) injection

TRYNGOLZA is injected subcutaneously once monthly via a convenient autoinjector[1,34]

In patients with sHTG[1]:

- The recommended dosage of TRYNGOLZA is **50 mg** once monthly with a low-fat diet
- Assess 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

TRYNGOLZA is self-administered once monthly into 1 of the following locations[1]:



Abdomen
Appropriate for self-injection

Front of the thigh
Appropriate for self-injection

Back of the upper arm
If a healthcare professional or caregiver administers the injection

- **If a dose is missed,** it should be administered as soon as possible after the missed dose. Resume dosing at monthly intervals from the date of the most recently administered dose[1]

Prior to initiation, train patients and/or caregivers on proper preparation and administration.[1]
For full details on administration and storage, see the Instructions for Use and the injection training video at TRYNGOLZAHCP.com.

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WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

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Getting patients started on TRYNGOLZA

Tryngolza® (olezarsen) injection

TRYNGOLZA can be prescribed using 1 of the 2 following options:

Electronically through your EHR

e-Prescribe TRYNGOLZA through your electronic health record (EHR) system to an in-network pharmacy*

OR

Fax the completed Start Form

Download the **TRYNGOLZA Start Form** or use the **Tear Pad** from your Account Specialist, then fax the completed form to an in-network pharmacy*

*Confirm if use of a specific specialty pharmacy is required by the patient's health insurance plan.

TRYNGOLZA is available through a network of select pharmacies.
Visit the website to learn more and to access helpful resources to get started.

IONIS EVERY STEP™ SUPPORT SERVICES

Ionis Every Step™ is committed to helping your patients access TRYNGOLZA.
For more information, call 1-844-789-8744, Monday to Friday, 8 AM to 8 PM ET.

SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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.

TRYNGOLZA is available through a select pharmacy network

Tryngolza® (olezarsen) injection

Use of a specific pharmacy may be required by some insurance plans or pharmacy benefit managers (PBMs), so it is important to confirm with the patient's plan prior to sending the prescription

Pharmacy	Phone number	Fax number	Website	Common payer/ PBM affiliations
Accredo	1-844-516-3319	1-888-302-1028	accredo.com/prescribers	Cigna, Express Scripts, Prime Therapeutics
BlinkRx	1-844-926-2480	1-866-585-4631	blinkrx.com/providers	Independent health plans
CVS Specialty	1-800-237-2767	1-800-323-2445	cvsspecialty.com	Aetna, CVS Health
Optum Specialty Pharmacy	1-855-427-4682	1-877-342-4596	specialty.optumrx.com	Optum Rx, UnitedHealthcare

Encourage your patient to save their pharmacy's number in their phone to help them recognize and answer the calls for setting up TRYNGOLZA delivery.

SELECT IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

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.

In patients with sHTG:

Achieve significant reductions in triglycerides and a longer time to first adjudicated acute pancreatitis events[1]

Tryngolza® (olezarsen) injection

TRYNGOLZA is a once-monthly, self-administered autoinjector with flexible dosing[1]

statistically significant mean change in fasting triglycerides with TRYNGOLZA 80 mg compared with placebo at Month 6 ($P<0.0001$); primary endpoint[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 ($P<0.0001$). 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]

reduction in the adjudicated acute pancreatitis event rate with TRYNGOLZA 50 mg compared with placebo[1†]

†In the integrated analysis of CORE and CORE2, TRYNGOLZA 50 mg and 80 mg demonstrated reductions of 91% (RR: 0.09; 95% CI: 0.02, 0.42) and 76% (RR: 0.24; 95% CI: 0.08, 0.69), respectively, in adjudicated acute pancreatitis event rates over 53 weeks compared with placebo. The pooled TRYNGOLZA group demonstrated an 85% reduction (RR: 0.15; 95% CI: 0.05, 0.40).[1]

of TRYNGOLZA-treated patients discontinued due to adverse reactions vs 2% of placebo-treated patients[1]

- **The most common adverse reactions (incidence ≥2% higher than placebo) were injection-site reactions and transaminases increased[1]**

Learn more about helping your patients get out of the danger zone at TRYNGOLZAHCP.com.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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