Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Olezarsen (chylomicronemia syndrome)

From 21 May 2026

At their session on 21 May 2026, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. In Annex XII, information on the active ingredient Olezarsen shall be added in alphabetical order as follows:

Olezarsen

Resolution of: 21 May 2026
Entry into force on: 21 May 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 17 September 2025):

Tryngolza is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS).

Therapeutic indication of the resolution (resolution of 21 May 2026):

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Olezarsen is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The G-BA determine the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of their Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

<u>Adults with genetically confirmed familial chylomicronemia syndrome (FCS)</u>

Extent of the additional benefit and significance of the evidence of olezarsen:

Indication of a minor additional benefit.

Study results according to endpoints:[1]

Adults with genetically confirmed familial chylomicronemia syndrome (FCS)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↑	Advantage in the "confirmed acute pancreatitis" endpoint.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↔	No relevant differences for the benefit assessment.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable		

Balance study: double-blind, randomised controlled phase III study, olezarsen 80 mg vs placebo, 53-week treatment period

Mortality

Endpoint	Olezarsen		Placebo		Olezarsen vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value
Overall survival					
No deaths occurred.					

[1] Data from the dossier assessment of the G-BA (published on 2 March 2026), and from the amendment to the dossier assessment from 24 April 2026, unless otherwise indicated.

Morbidity

Endpoint	Olezarsen			Placebo			Olezarsen vs placebo
	N	Patients with at least one event n (%)	Total number of events	N	Patients with at least one event n (%)	Total number of events	RR[b] [95% CI] p value
Confirmed acute pancreatitis (AP)[a] up to month 12	22[c]	1 (4.50)	1	23[c]	7 (30.4)	11	0.68 [0.49; 0.95] 0.009

Endpoint	Olezarsen			Placebo			Olezarsen vs placebo
	N	Patients with at least one event n (%)	Total number of events	N	Patients with at least one event n (%)	Total number of events	RR [95% CI] p value
Hospitalisation							
Total hospitalisation	22	3 (13.6)	3	23	9 (39.1)	17	0.35 [0.11; 1.12] 0.073[d]
Hospitalisations due to AP *(presented additionally)*	22	1 (4.50)	1	23	7 (30.4)	11	0.68 [0.49; 0.95] 0.009[b]

Endpoint	Olezarsen			Placebo			Olezarsen vs placebo
	N	Patients with event n (%)		N	Patients with event n (%)		RR [95% CI] p value
Symptomatology using FCS-SIS (FCS symptom)[e]							
Deterioration[h]	17[f]	1 (5.90)		20[f]	1 (5.0)		1.05 [0.91; 1.20] 0.60[g]
Improvement[h] *(presented additionally)*[w]	17[f]	0 (0)		20[f]	0 (0)		-
Symptom severity using the PGIS[y]							
Deterioration[x]	15[f]	3 (20.0)		18[f]	2 (11.1%)		1.11 [0.81; 1.51] 0.90[b]
Improvement[x] *(presented additionally)*[w]	16[z]	3 (18.8)		19[z]	5 (26.3)		0.90 [0.64; 1.28] 0.59[b]
	N	Baseline MV (SD)	Change at month 12 LS mean [95% CI]	N	Baseline MV (SD)	Change at month 12 LS mean [95% CI]	LS mean difference [95% CI] p value[v]
Fasting triglyceride level (mg/dl) *(presented additionally)*	22	2.613 (1.499)	-38.5 [-58.2; -18.8]	23	2.596 (1.256)	20.89 [1.02; 40.8]	-59.4 [-90.7; -28.1] 0.0002

Health-related quality of life

Endpoint	Olezarsen		Placebo		Olezarsen vs placebo
	N[f]	Patients with event n (%)	N[f]	Patients with event n (%)	RR [95% CI] p value[h]
FCS-SIS (FCS-Impact)[i]					
Deterioration[j]	17	2 (11.8)	21	4 (19.0)	0.89 [0.66; 1.19] 0.41
Improvement[j] *(presented additionally)*[w]	17	2 (11.8)	21	4 (19.0)	1.00 [0.73; 1.32] 0.89

	N[l]	Baseline[m] MV (SD)	Change from baseline to month 12[n] LS mean [95% CI]	N[l]	Baseline[m] MV (SD)	Change at month 12[n] to baseline LS mean [95% CI]	LS mean difference [95% CI] p value
PROMIS-29[k]							
Physical component summary score	No data available.						
Mental component summary score	No data available.						
Single domains							
Physical functions[o]	15	47.8 (9.36)	1.67 (9.30)	18	48.5 (10.4)	0.66 (4.08)	0.25 [-4.07; 4.56] 0.91
Fears/ worries[p]	15	58.3 (11.9)	-1.80 (9.83)	18	55.8 (11.6)	-0.33 (5.55)	-0.12 [-6.01; 5.78] 0.97
Depression[p]	15	51.9 (12.1)	0.30 (9.84)	18	51.8 (10.3)	-2.20 (7.67)	3.32 [-2.56; 9.19] 0.26
Fatigue[p]	15	51.2 (11.9)	0.17 (7.86)	18	51.7 (12.6)	-0.37 (3.76)	1.14 [-3.23; 5.51] 0.60
Pain-related impairment[p]	18	53.0 (12.6)	-2.81 (10.5)	21	52.5 (11.8)	-2.86 (7.94)	0.83 [-4.28; 5.94] 0.75
Sleep disorders[p]	15	50.2 (8.25)	-2.86 (8.17)	18	49.0 (8.21)	1.84 (7.13)	-2.79 [-8.77; 3.19] 0.35
Ability to participate in social activities[o]	15	50.7 (10.6)	0.71 (7.48)	18	50.8 (12.4)	1.72 (6.20)	-1.88 [-6.66; 2.91] 0.43
PROMIS Short Form – Pain Interference 8a *(presented additionally)*							
	18	53.1 (13.4)	-2.04 (11.5)	22	52.7 (12.5)	-3.16 (7.9)	2.46 [-2.62; 7.53] 0.34

Side effects

Endpoint MedDRA system organ classes/ AE of special interest	Olezarsen		Placebo		Olezarsen vs placebo
	N[q]	Patients with at least one event n (%)	N[q]	Patients with at least one event n (%)	RR [95% CI]; p value[r]
Total adverse events (presented additionally)	22	19 (86.4)	23	22 (95.7)	-
Severe adverse events (CTCAE grade 3 or 4)	22	1 (4.50)	23	9 (39.1)	0.12 [0.02; 0.84] 0.01
Severe adverse events (CTCAE grade 3 or 4) - without pancreatitis PTs[s]	22	0 (0)	23	6 (26.1)	0.08 [0.00; 1.35] 0.02
Serious adverse events (SAEs)	22	3 (13.6)	23	9 (39.1)	0.35 [0.11; 1.12] 0.09
Serious adverse events (SAEs) - without pancreatitis PTs[s]	22	2 (9.1)	23	5 (21.7)	0.42 [0.09; 1.94] 0.41
Therapy discontinuation due to adverse events	22	2 (9.10)	23	0 (0)	5.22 [0.26; 102.9] 0.23
MACE[t]	22	1 (4.50)	23	1 (4.35)	n.d.[u]
Severe adverse events according to MedDRA-SOC (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms)					
Gastrointestinal disorders	22	1 (4.50)	23	7 (30.4)	0.15 [0.02; 1.12] 0.047
Gastrointestinal disorders - without pancreatitis PTs[s]	22	0 (0)	23	3 (13.0)	0.15 [0.01; 2.73] 0.23
SAEs according to MedDRA-SOC (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms)					
Gastrointestinal disorders	22	2 (9.1)	23	9 (39.1)	0.23 [0.06; 0.96] 0.04
Gastrointestinal disorders - without pancreatitis PTs[s]	22	1 (4.5)	23	2 (8.7)	0.52 [0.05; 5.36] 1.00

a. Confirmed AP for the analysis was defined as documented, probable and possible AP according to the committee's assessment.
b. RR and p value stratified by both stratification factors: "history of pancreatitis within 10 years prior to screening" (yes/ no) and "pretreatment with volanesorsen" (yes/ no). An exact calculation of the p value is not described.

c. Three subjects in the olezarsen arm (13.6%) and one subject in the placebo arm (4.3%) discontinued treatment up to month 12 and were not included fully in the analysis.
d. Own calculation: exact test without taking stratification factors into account
e. The scale range is from 0 to 10. Higher values indicate more severe FCS symptoms.
f. Returns at week 53.
g. RR and p value stratified by both stratification factors: "history of pancreatitis within 10 years prior to screening" (yes/ no) and "pretreatment with volanesorsen" (yes/ no). Missing data were not imputed. An exact calculation of the p value is not described.
h. Deterioration is defined as an increase in the FCS total symptom score by ≥ 15% of the scale range at month 12.
i. The scale range is from 0 to 4. Higher values indicate greater FCS burden.
j. Deterioration is defined as an increase in the FCS total impact score by ≥ 15% of the scale range at month 12.
k. The pharmaceutical company presented the PROMIS 29+2 in the dossier. No suitable studies on validity are available for the addition of a domain on cognitive functioning comprising 2 items; consequently, the results of the validated PROMIS-29 questionnaire are used here for the benefit assessment.
l. The number corresponds to those subjects who were included in the analysis of change up to month 12.
m. Baseline is defined as the last non-missing measurement prior to the administration of the first dose of the study medication.
n. Change at month 12 using an ANCOVA model with treatment group and the stratification factors "pancreatitis in the last 10 years" (yes/ no) and "pretreatment with volanesorsen" (yes/ no) as fixed effects, and the respective domain scores at baseline as covariates.
o. Based on t-transformed values with a mean value of 50 and an SD of 10. Values below 50 indicate a greater degree of impairment.
p. Based on t-transformed values with a mean value of 50 and an SD of 10. Values above 50 indicate a greater degree of restriction.
q. The number corresponds to the safety population.
r. Calculation using Fisher's exact test. The stratification factors were not taken into account.
s. Pancreatitis, necrotising pancreatitis, acute pancreatitis, chronic pancreatitis
t. Assignment of the MACE endpoint to the safety endpoint category is unclear.
u. No effect estimators (with corresponding p value) were provided in the dossier. Due to the number of events, no statistically significant difference between the treatment arms is assumed.
v. p values and 95% CI using the robust variance estimator according to Bell and McCaffrey.
w. As around a quarter of subjects in the olezarsen arm and a third of subjects in the placebo arm showed no symptoms at baseline and therefore could not show any improvement, responder analyses of deterioration in this study population are considered to be of primary relevance as opposed to analyses of improvement.
x. Improvement defined as a change in the PGIS compared to baseline < 0. Deterioration defined as a change in the PGIS compared to baseline > 0.
y. The scale range is from 0 to 4; higher values indicate more severe FCS symptoms.
z. Month 12 is pre-specified as the mean value of weeks 51 and 53. Based on the available data, it is assumed that this analysis corresponds to a responder analysis at week 53 compared to baseline.

Abbreviations used:

ANCOVA: analysis of covariance; AP: acute pancreatitis; CTCAE: Common Terminology Criteria for Adverse Events; FAS: full analysis set; FCS: familial chylomicronemia syndrome; FCS-SIS: FCS Symptoms and Impacts Scale; HR: hazard ratio; J2R: jump to reference; n.d.: no data available; CI: confidence interval; LS: least squares; LSM: least squares means; MACE: major adverse cardiovascular events; MAR: missing at random; MedDRA: Medical Dictionary for Regulatory Activities; MI: multiple imputation; MV: mean value; n.a.: not assessable; PGIS: Patient Global Impression of Severity; PROMIS: Patient-Reported Outcomes Measurement Information System; RR: relative risk; SD: standard deviation; SMD: standardised mean difference; (S)AE: (serious) adverse event; TG: triglyceride.

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with genetically confirmed familial chylomicronemia syndrome (FCS)

Approx. 60 to 130 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Tryngolza (active ingredient: olezarsen) at the following publicly accessible link (last access: 15 April 2026):

https://www.ema.europa.eu/en/documents/product-information/tryngolza-epar-product-information_en.pdf

4. Treatment costs

Annual treatment costs:

Adults with genetically confirmed familial chylomicronemia syndrome (FCS)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Olezarsen	€ 337,185.00

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 March 2026)

Costs for additionally required SHI services: not applicable

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Adults with genetically confirmed familial chylomicronemia syndrome (FCS)

- No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between statutory health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

6. Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Tryngolza is a medicinal product placed on the market from 1 January 2025.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5 per cent of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant percentage within the scope of SGB V.

II. The resolution will enter into force on the day of its publication on the G-BA website on 21 May 2026.

The justification for this resolution will be published on the G-BA website at www.g-ba.de.

Berlin, 21 May 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken