Report TRYNGOLZA® - Olezarsen

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Olezarsen **Brand Name:** Tryngolza **Originator/licensee:** Ionis Ireland Limited **Classification:** NCE **ATC code:** C10AX **Orphan Status:** **Eu:** Yes **Us:** Yes **Mechanism of action:** Olezarsen, a lipid modifying agent, is an antisense oligonucleotide which inhibits the formation of apolipoprotein C3, a protein that regulates both triglyceride metabolism and hepatic clearance of chylomicrons and other triglyceride-rich lipoproteins. By reducing serum apolipoprotein C3, olezarsen increases clearance of plasma triglycerides [1].	**Authorized Indication:** **EMA**: Olezarsen is indicated as an adjunct to diet in adults for the treatment of genetically confirmed FCS [1]. **FDA:** Olezarsen is indicated as an adjunct to diet to reduce triglycerides in adults with familial FCS [2]. **Route of administration:** SC **Licensing status** **EU CHMP P.O. date:** 24/07/2025 **FDA M.A. date:** 19/12/2024 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** Yes --- **ABBREVIATIONS:** **AE**: Adverse Event **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **FCS**: Familial chylomicronemia syndrome **HR**: Hazard Ratio **M.A.**: Marketing Authorization **P.O.**: Positive Opinion **PS**: Performance Status **Pts**: Patients **SAE**: Serious adverse events **SC**: Subcutaneously **TEAE**: Treatment-emergent related AEs **WHO**: World Health Organization	**Summary of clinical EFFICACY:** **Balance (NCT04568434)** was a multicentre, double-blind, placebo-controlled, phase III trial that evaluated the efficacy and safety of olezarsen, as compared with placebo, among pts. who had FCS. Eligible pts. were ≥18 years of age, with diagnosis of FCS and fasting triglyceride levels of ≥880 mg/dL. Pts. who had previously received volanesorsen were eligible to be enrolled (all the pts. included had not received volanesorsen for ≥1 year before randomization). It was determined whether the pt. has been maintaining a stable diet; if not, the pt was enrolled in a 2-week dietary run-in period. Pts. were instructed to follow a low-fat diet with ≤20 grams fat per day. Pts. (n=66) were randomly assigned in a 2:1 ratio, to receive olezarsen (n=43) at the dose of 80 mg (n=22) or 50mg (n=21) or placebo (n=23). Randomization was stratified according to history of pancreatitis and previous treatment with volanesorsen. Treatment was administered subcutaneously every four weeks for 49 weeks. The two primary end points were the difference between the 80-mg olezarsen group and the placebo group in the percent change in the fasting triglyceride level from baseline to six months, and the difference between the 50-mg olezarsen group and the placebo group (to be assessed if the first was significant). In pts. treated with olezarsen 80 mg, a significant reduction was observed compared to placebo, with a mean difference of −43.5% (95% CI: −69.1% to −17.9%; $p < 0.001$). On the contrary, the reduction observed with 50 mg did not reach statistical significance ($p = 0.08$) [3]. **Summary of clinical SAFETY:** Moderate severity AEs considered to be related to the trial drug or placebo occurred in four pts. (18%) in the 80-mg olezarsen group (chills, myalgia, and trismus; chest discomfort, diarrhoea, flushing, and vomiting; transient decrease in the platelet count; alopecia). Three pts. (two in the 80-mg olezarsen group and one in the 50-mg olezarsen group) reported AEs that led to treatment discontinuation. One death occurred in the 50-mg olezarsen group, that has been considered unrelated to the trial treatment the investigators [3]. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** No **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/medicines/human/EPAR/tryngolza [2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218614s000lbl.pdf [3] https://www.nejm.org/doi/full/10.1056/NEJMoa2400201 [4] https://www.orpha.net/en/disease/detail/444490 [5] https://link.springer.com/article/10.1007/s11883-025-01295-x	**Cost of therapy:** Not available yet. **Epidemiology:** FCS has an estimated prevalence of 1/300,000 (ranging from 1/100,000 to 1/1,000,000 in Europe and North America) [4]. --- **POSSIBLE PLACE IN THERAPY**: Restricting dietary fat remains the cornerstone to treat FCS due to the failure of conventional therapies (statins, fibrates, niacin, etc.). This includes limiting dietary fat intake to 5-10% of total daily calories and incorporating medium-chain triglycerides to reduce chylomicron production. New therapies, such as antisense oligonucleotide and small interfering RNA targeting apolipoprotein C3 and Angiopoietin-like Protein 3, are considered emerging approaches [5]. The addition of Olezarsen to the above regimens could represent a new opportunity for these pts. **OTHER INDICATIONS IN DEVELOPMENT: -** **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Plozasiran (NCT05089084; NCT05902598) *Service reorganization: No *Possible off label use: Yes

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