**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Olezarsen for treating familial chylomicronaemia syndrome

**Final scope**

## Remit/evaluation objective

To appraise the clinical and cost effectiveness of olezarsen within its marketing authorisation for treating familial chylomicronaemia syndrome.

## Background

Familial chylomicronaemia syndrome (FCS) is a rare genetic disorder caused by mutations in one or more genes. These mutations cause an absence or a deficiency of the enzyme lipoprotein lipase, which breaks down fat in the diet. This results in very high levels of triglycerides, a kind of fat, in the blood and a build-up of chylomicrons (the particles responsible for transporting dietary fat from the intestine to the rest of the body). Symptoms of FCS include moderate to severe abdominal pain, unpredictable and recurrent episodes of acute pancreatitis, liver and spleen enlargement, eruptive xanthomas (yellow, fatty skin deposits), reduced cognition, and fatigue. FCS also has a substantial psychological impact. FCS can lead to serious health problems in the long term, including chronic pancreatitis and diabetes.

The prevalence of FCS is around 1 to 2 per million people[1], which equated to around 57 to 114 people in England in 2022.[2]

FCS is managed by an extremely restrictive, very low-fat diet to keep triglyceride levels low. This involves restricting dietary fat intake to between 10 and 20 g/day, and not consuming alcohol. Because of the restricted diet, people also require supplements of essential fatty acids (linoleic and alpha linolenic acids) and fat soluble vitamins (A, D, E and K). The strict dietary regimen can be very challenging and many people still have high triglyceride levels even when the diet is closely followed. Lipid-lowering treatments such as fibrates, statins and omega-3 fatty acids may also be tried, but these are mimimally effective.

NICE Highly Specialised Technologies guidance 13 recommends volanesorsen within its marketing authorisation, as an option for treating genetically confirmed FCS in adults who are at high risk of pancreatitis, and when response to diet and triglyceride-lowering therapy has been inadequate.

## The technology

Olezarsen (Tryngolza, Sobi) does not currently have a marketing authorisation in the UK for treating FCS. It has been studied in a clinical trial compared with placebo in adults with genetically confirmed FCS and fasting triglycerides levels of 880mg/dl (10mmol/L) or above with a history of pancreatitis. People without a documented history of pancreatitis were also eligible but their enrolment was capped at 35%. It has also been studied in a clinical trial in people who are currently having or who have had volanesorsen.

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| **Intervention** | Olezarsen |
| **Population(s)** | Adults with familial chylomicronaemia syndrome |
| **Subgroups** | • Triglyceride levels<br>• History of pancreatitis<br>• People with diabetes<br>• People who cannot have volanesorsen<br>• Pregnancy |
| **Comparators** | • Volanesorsen<br>• Plozasiran (subject to NICE evaluation)<br>For people who cannot have volanesorsen:<br>• Established clinical management without olezarsen (including dietary fat restriction) |
| **Outcomes** | The outcome measures to be considered include:<br>• triglyceride levels<br>• chylomicron levels<br>• APOC3 levels<br>• abdominal pain<br>• fatigue<br>• neurological and psychological impact of disease (including depression and cognitive ability)<br>• incidence of acute pancreatitis, chronic pancreatitis, diabetes and other complications (including pancreatic necrosis)<br>• hospitalisation (including admissions to intensive care units; all-cause and pancreatitis-related admissions)<br>• incidence of severe thrombocytopenia<br>• monitoring requirements<br>• adherence<br>• mortality (including all-cause and pancreatitis-related mortality)<br>• adverse effects of treatment<br>• health-related quality of life (for patients and carers) |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be |

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| | sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br><br>The economic modelling should include the costs associated with diagnostic testing in people with FCS who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation). |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations** | **Related highly specialised technology appraisals:**<br><br>Volanesorsen for treating familial chylomicronaemia syndrome (2020) NICE highly specialised technology guidance 13.<br><br>**Related technology appraisals in development:**<br><br>Plozasiran for treating familial chylomicronaemia syndrome. NICE technology appraisal guidance [ID6593]. Publication date to be confirmed. |

**References:**

1. Heart UK (2025). Familial chylomicronaemia syndrome. Accessed 30 June 2025.

2. Office for National Statistics (2023). Population estimates for the UK, England, Wales, Scotland and Northern Ireland: mid-2023. Accessed 30 June 2025.