NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Olezarsen for treating familial chylomicronaemia syndrome ID6585

Draft scope

Draft 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 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 equates 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, nicotinic acids, 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.

Intervention	Olezarsen
Population(s)	Adults with familial chylomicronaemia syndrome
Subgroups	• Triglyceride levels • History of pancreatitis • Risk of pancreatitis • Previous treatment with volanesorsen
Comparators	• Established clinical management without olezarsen (including dietary fat restriction) • Volanesorsen • Plozasiran (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • chylomicron and triglyceride levels • abdominal pain • fatigue • neurological and psychological impact of disease (including depression and cognitive ability) • incidence of acute pancreatitis, chronic pancreatitis, diabetes and other complications (including pancreatic necrosis, fatty liver disease and cardiovascular disease) • hospitalisation (including admissions to intensive care units; all-cause and pancreatitis-related admissions) • mortality (including all-cause and pancreatitis-related mortality) • adverse effects of treatment • 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. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

	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:** Volanesorsen for treating familial chylomicronaemia syndrome (2020) NICE highly specialised technology guidance 13. **Related technology appraisals in development:** Plozasiran for treating familial chylomicronaemia syndrome. NICE technology appraisal guidance [ID6593]. Publication date to be confirmed.

Questions for consultation

Where do you consider olezarsen will fit into the existing care pathway for familial chylomicronaemia syndrome?

Please select from the following, will olezarsen be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would olezarsen be a candidate for managed access?

Do you consider that the use of olezarsen can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which the treatment will be licenced licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

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.