NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Triheptanoin for treating long-chain fatty acid oxidation disorders

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of triheptanoin within its marketing authorisation for treating long-chain fatty acid oxidation disorders.

Background

Long-chain fatty acid oxidation disorders (LC-FAODs) are a group of genetic disorders characterised by acute crises of energy production and chronic energy deficiency. LC-FAODs are caused by mutations in the genes that contain the genetic code to make enzymes that allow for long-chain fatty acids to be converted into energy. Symptoms of LC-FAODs can include rhabdomyolysis (breakdown of muscle) induced by exercise, fasting or illness, liver dysfunction, and cardiomyopathy, although symptoms and severity can vary between types of LC-FAOD[1]. There are 5 main types of LC-FAOD, depending on which mutation is present, which are:

- Carnitine palmitoyltransferase I (CPT I) deficiency
- Carnitine palmitoyltransferase II (CPT II) deficiency
- Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency
- Long-chain 3-hydroxy-acyl-CoA dehydrogenase (LCHAD) deficiency
- Trifunctional protein (TFP) deficiency[1]

The prevalence of LC-FAOD is difficult to estimate because some people may be asymptomatic or pre-symptomatic and are therefore unidentified. Newborn screening programmes estimate the incidence of LC-FAOD across Australia, Germany, and USA (combined) was between 1:47,398 and 1:53,769 births[2]. A study suggests this would equate to 476 patients in the UK with approximately half of them diagnosed[3].

Treatment for LC-FAODs involves avoiding fasting, providing aggressive management during illness, and possible supplementation with carnitine, if deficient. LC-FAODs differ from other fatty-acid metabolism disorders by requiring a fat restricted diet, potentially a higher protein intake, and supplementation of medium-chain triglyceride (MCT) oil.

The technology

Triheptanoin (Dojolvi, Ultragenyx) does not currently have a marketing authorisation for treating LC-FAODs. It has been studied in clinical trials compared with MCT oil in people with LC-FAODs.

Intervention	Triheptanoin
Population	People with long-chain fatty acid oxidation disorders
Comparators	Established clinical management without triheptanoin including: • medium-chain triglyceride oil
Outcomes	The outcome measures to be considered include: • mortality • major clinical events • hospitalisations • adverse effects of treatment • health-related quality of life.
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.
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	None
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 62, Specialist metabolic disorder services (adults and children)

Questions for consultation

What is included in the typical management of LC-FAODs?

Could the type of LC-FAOD affect the efficacy of treatment with triheptanoin?

Are there symptoms common to all LC-FAODs?

Where do you consider triheptanoin will fit into the existing care pathway for LC-FAODs?

Please select from the following, will triheptanoin 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 triheptanoin be a candidate for managed access?

Do you consider that the use of triheptanoin 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.

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 triheptanoin will be 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. Vockley, J. (2020). Long-Chain Fatty Acid Oxidation Disorders and Current Management Strategies. American Journal Of Managed Care 26(7 Suppl): S147-154

2. Lindner, M., Hoffmann, G.F., and Matern, D. (2010). Newborn screening for disorders of fatty-acid oxidation: experience and recommendations from an expert meeting. Journal of Inherited Metabolic Disease 33(5):pg521-526
3. Kruger, E., McNiven, P., Thomas, N.A., and Marsden, D. (2020). PRO108 Method for Estimating Disease Frequency in Long Chain Fatty Acid Oxidation Disorders and Forecasting Future Trends in Europe