**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Elamipretide for treating Barth syndrome in people of any age ID6545

**Draft scope**

## Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of elamipretide within its marketing authorisation for treating Barth syndrome in people of any age.

## Background

Barth syndrome is a genetic condition caused by a mutation in the tafazzin (TAZ) gene thats helps maintain mitochondrial function. The mutation impairs mitochondrial energy production in the body and mainly affects the heart and skeletal muscles. Barth syndrome is caused by an X-linked recessive gene and more prevalent in men, trans women and non-binary people registered male at birth.[1-3]

The estimated prevalence of Barth syndrome is 1 in 454,000 and incidence is 1 in 140,000 using data from South-West England and South Wales (Orphanet category 1-9/1,000,000)).[2,4-5] Approximately 230-250 cases have been identified worldwide.[3-4]

Diagnosis of Barth syndrome includes a combination of clinical characteristics followed by a genetic test. These can include cardiolipin analysis, urine organic acid analysis including quantification of 3-methylglutaconic acid (Type II), complete blood count and differential, echocardiogram, analysis of growth parameters from birth and TAZ gene sequencing.[6-7] The main symptoms include heart muscle weakness (cardiomyopathy), skeletal muscle weakness (skeletal myopathy), lack of white blood cells (neutropenia), fatigue, exercise intolerance, feeding issues and growth delays.[8-9.]

Early diagnosis, effective management of severe neutropenia and cardiac risk factors can determine life expectancy in this population.[3,10-11]The estimated 1-year survival rate with and without severe neutropenia at time of diagnosis is 25% and 68% respectively. The reported 5-year survival rate pre-2000 is 22% and post-2000 is 70%.[11] Birth year correlates with better prognosis because of early diagnosis and treatment of heart failure.[3,11]

There are currently no treatment options for Barth syndrome. The clinical management includes a multidisciplinary approach to treating the main symptoms of Barth syndrome and can include the following:[1,12]

- Heart failure or cardiomyopathy: cardiac management, including heart transplant in severe cases
- Neutropenia: infection-risk management, can include Granulocyte Colony Stimulating Factor and prophylactic antibiotics
- Growth delay: nutritional and metabolic support

- Skeletal myopathy: rehabilitation and functional support, including physiotherapy and exercise training

**The technology**

Elamipretide (Brand name TBC, Pharmanovia) does not currently have a marketing authorisation in the UK for Barth syndrome in people of any age. It has been studied in a clinical trial in which elamipretide has been compared with placebo in people aged 12 and above, with genetically confirmed Barth syndrome who have not had a heart transplant.

| | |
|---|---|
| **Intervention(s)** | Elamipretide |
| **Population(s)** | People of any age with genetically confirmed Barth syndrome |
| **Subgroups** | If evidence allows, subgroups by age, disease severity, or treatment history may be considered<br>For example:<br>Age:<br>• infants and young children<br>• older children and adolescnets<br>• adults<br>Disease severity:<br>• mild<br>• severe<br>History of heart transplant:<br>• pre-transplant<br>• post-transplant |
| **Comparators** | Current standard care for Barth Syndrome in the NHS, including but not limited to:<br>• Cardiac management<br>• Infection-risk management<br>• Nutritional and metabolic support<br>• Rehabilitation and functional support |

| | |
|---|---|
| **Outcomes** | The outcome measures to be considered include:<br>• disease progression<br>• response to treatment (for example physical capacity or exercise tests)<br>• improvements in symptoms, including fatigue<br>• adverse effects of treatment<br>• health-related quality of life<br>• mortality |
| **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 sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br>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 |

**Questions for consultation**

How is Barth syndrome diagnosed in the NHS, and at what age are people with Barth syndrome usually diagnosed?

Is the population defined properly in the draft scope?

How is genetically confirmed Barth syndrome managed in the NHS?

How are the main symptoms associated with genetically confirmed Barth syndrome managed in the NHS. Symptoms include but are not limited to:

- Cardiomyopathy
- Skeletal myopathy
- Neutropenia and infections

What proportion of people with genetically confirmed Barth syndrome need a heart transplant in the NHS?

If elamipretide is recommended, can people who had a heart transplant also be offered this treatment?

Where do you consider elamipretide will fit into the existing care pathway for Barth syndrome? Are there any specific comparators that should be considered within this scope?

Do you expect elamipretide to be offered as an add-on treatment to current treatments that are used to manage Barth syndrome?

Are there any other subgroups that may need to be considered?

What is the average life expectancy for people with genetically confirmed Barth syndrome in England?

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

Do you consider that the use of elamipretide 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 comment on the outcome measures listed in the scope and if any additional outcomes should be considered that are not in the list?

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 elamipretide 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. Barth Syndrome UK, website link: https://www.barthsyndrome.org.uk/ (accessed: 06.02.2026)

2. https://www.orpha.net/ (Barth Syndrome) (accessed: 06.02.2026)

3. Ferreira C, Pierre G, Thompson R, et al. Barth Syndrome. 2014 Oct 9 [Updated 2026 Jan 8]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK247162/

4. Miller, Paighton C., et al. "A Bayesian analysis to determine the prevalence of Barth syndrome in the pediatric population." The Journal of pediatrics 217 (2020): 139-144.

5. Clarke, Sarah LN, et al. "Barth syndrome." Orphanet journal of rare diseases 8.1 (2013): 23.

6. NHS University Hospitals Bristol, NHS Foundation Trust, website link: NHS National Barth Syndrome Service (accessed: 06.02.2026)

7. Barth Syndrome Foundation, Approaches to Diagnosis, website link: Clinical Manifestations of Barth Syndrome (accessed: 06.02.2026)

8. Kenneson A, Huang Y, Lontok E, Marjoram L. The diagnostic odyssey, clinical burden, and natural history of Barth syndrome: an analysis of patient registry data. J Transl Genet Genom. 2024;8:285-97. http://dx.doi.org/10.20517/jtgg.2024.22

9. Sergi, C.M. Barth Syndrome: *TAFAZZIN* Gene, Cardiologic Aspects, and Mitochondrial Studies—A Comprehensive Narrative Review. *Genes* **2025**, *16*, 465. https://doi.org/10.3390/genes16040465

10. Chowdhury, S., Jackson, L., Byrne, B.J. *et al.* Longitudinal Observational Study of Cardiac Outcome Risk Factor Prediction in Children, Adolescents, and Adults with Barth Syndrome. *Pediatr Cardiol* **43**, 1251–1263 (2022). https://doi.org/10.1007/s00246-022-02846-8

11. Rigaud C, Lebre AS, Touraine R, Beaupain B, Ottolenghi C, Chabli A, Ansquer H, Ozsahin H, Di Filippo S, De Lonlay P, Borm B, Rivier F, Vaillant MC, Mathieu-Dramard M, Goldenberg A, Viot G, Charron P, Rio M, Bonnet D, Donadieu J. Natural history of Barth syndrome: a national cohort study of 22 patients. Orphanet J Rare Dis. 2013 May 8;8:70. doi: 10.1186/1750-1172-8-70.

12. Thompson R, Jefferies J, Wang S, et al. Current and future treatment approaches for Barth syndrome. *J Inherit Metab Dis*. 2022; 45(1): 17-28. doi:**10.1002/jimd.12453**