Oscar Clinical Guideline: Forzinity (elamipretide) (PG274, Ver. 1)

Forzinity (elamipretide)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Barth syndrome (BTHS) is a very rare genetic condition characterized by mitochondrial abnormalities. These abnormalities lead to exercise intolerance, muscle weakness, debilitating fatigue, cardiomyopathy, heart failure, recurrent infections, and delayed growth. Barth syndrome is inherited in an X-linked manner and mostly affects males.

Males with Barth syndrome have a reduced life expectancy. The highest mortality risk occurs during infancy or early childhood. Complications of heart failure or infection lead to death in infancy or early childhood. Those who live into adulthood can survive into their late forties.

Definitions

"6-minute walk test (6MWT)" is an objective measure of submaximal exercise capacity. It quantifies the distance an individual is able to walk on a flat, hard surface over a period of 6 minutes.

"Barth Syndrome Symptom Assessment (BTHS-SA)" is 3-question fatigue assessment using a 0- to 4-point scale for each question, where no fatigue = 0 and very severe fatigue = 4, with scores from all 3 questions combined and averaged. The combined minimum score = 0 to maximum score = 12. A lower score means a better outcome, a higher score means a worse outcome.

"Confirmatory trials" refers to additional clinical trials conducted to validate or confirm the results of previous studies, typically designed to replicate findings and further establish the clinical benefit and safety profile of a treatment.

"Efficacy information" refers to data that demonstrates the effectiveness or therapeutic benefits of a medication or intervention in treating a specific condition.

"Long-term outcomes" refers to the effects, benefits, or adverse events observed over an extended period of time, usually beyond the duration of a clinical trial, providing insights into the sustained efficacy and safety of a treatment.

"Open-label extension study" is a continuation of a clinical trial where patients who completed the original trial are offered the study drug or treatment under open-label conditions.

"Robust evidence" means strong, reliable, and conclusive evidence derived from well-designed and well-conducted clinical studies, often including randomized controlled trials, systematic reviews, and meta-analyses.

"Statistically significant" is a term used to describe results that are unlikely to have occurred by chance and are considered meaningful from a statistical perspective.

"[s]" indicates state mandates may apply.

Policy Statement on Forzinity (elamipretide) Efficacy Information[5]

The use of Forzinity (elamipretide) is considered unproven and therefore not medically necessary for the treatment of Barth syndrome or any other indication. While Forzinity (elamipretide) has received FDA accelerated approval based on knee extensor muscle strength, the available clinical evidence does not demonstrate that it provides clinically meaningful benefits in terms of slowing disease progression.

- TAZPOWER/SPIBA-201, Part 1 (NCT03098797) was a phase 2, 28 week, randomized, double-blind, placebo-controlled, crossover trial evaluating Forzinity subcutaneous (SC) injections in 12 participants. The primary endpoints were distance walked [in meters (m)] during the 6-minute walk test (6MWT) and Total Fatigue Score based on Barth Syndrome Symptom Assessment (BTHS-SA). After 12 weeks of Forzinity therapy, a statistical difference was not observed in distance walked on the 6MWT vs. placebo (-0.8 m, p = 0.97). A statistical difference was also not observed in the BTHS-SA Total Fatigue Score vs. placebo (+0.06; p = 0.89). A sequence effect was not observed for either primary endpoint. Statistical differences were not observed for secondary endpoints.
- TAZPOWER Extension/SPIBA-201, Part 2 (NCT03098797) was a single-arm open-label extension (OLE) evaluating Forzinity for up to 192 weeks. The primary endpoint was long-term safety and tolerability of single, daily doses of 40 mg Forzinity. From Part 1, 8 of 10 patients participated through week 168. Increases in knee extensor muscle strength (not observed during the randomized trial) were observed during the extension period. Public communications have cited ~45% improvement from open-label analyses. There were improvements in 6MWT and BTHS-SA observed. The 6MWT gains were +60.5 m (16%; p = 0.02) at week 12 and +95.9 m (25%; p = 0.02) at week 36. BTHS-SA Total Fatigue Score decreases were observed the mean improvement was -1.6 points [19% improvement, p = 0.03]) at week 12 and mean improvement of -2.1 points [26% improvement, p = 0.03]) at week 36. Limitations of this study include the open-label design and limited number of participants. Results cannot be interpreted as a treatment effect due to the nature of an open-label design as the magnitude of benefit compared to placebo is unknown. Additionally, knee extensor muscle strength observed in the clinical trial has not been validated as a surrogate endpoint for clinical benefit in Barth syndrome.
- SPIBA-001/NHC Trial was a trial to assess the efficacy of Forzinity (N = 10) vs. retrospective external control the natural history control (NHC). The primary endpoint was the change from baseline in mean distance on the 6MWT to weeks 64 and 76. For 6MWT, the least squares (LS) mean difference between groups was 79.7 m (p = 0.0004) at week 64 and 91.0 m (p = 0.0005) at week 76 favoring Forzinity. Limitations include the observational nature of this study design and the limited number of participants. Additionally, the 6MWT is effort-dependent, has intra-subject variability, and is difficult to interpret based on comparisons with an external, historical control group, particularly given the lack of statistical significance against placebo in TAZPOWER Part 1.

Clinical Indications

Medical Necessity Criteria for Clinical Review[s]

General Medical Necessity Criteria

Indication-Specific Criteria

Barth Syndrome

Due to the uncertain clinical evidence, the Plan does not have standard medical necessity criteria for Forzinity (elamipretide) at this time. Coverage for Forzinity (elamipretide) for members to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg will be determined on a case-by-case basis.

Experimental or Investigational or Unproven / Not Medically Necessary[s]

Forzinity (elamipretide) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, unproven, or not medically necessary. The Plan has determined that the available evidence does not support the clinical efficacy, safety, or medical necessity of Forzinity (elamipretide) at this time.

The Plan will continue to monitor emerging evidence, including results from ongoing clinical trials, and will reassess its position as new data become available..

Applicable Billing Codes

Table 1	
CPT/HCPCS codes considered NOT medically necessary:	
Code	*Description*
C9399	Forzinity Unclassified drugs or biologicals
J3490	Forzinity Unclassified drugs

Table 2	
ICD-10 diagnosis codes considered NOT medically necessary with Table 1 (CPT/HCPCS) codes:	
Code	*Description*
E78.71	Barth Syndrome

References

1. ClinicalTrials.gov. A Trial to Evaluate Safety, Tolerability and Efficacy of Elamipretide in Subjects With Barth Syndrome (TAZPOWER). Available at: https://clinicaltrials.gov/study/NCT03098797. Accessed November 14, 2025.
2. Ferreira C, Pierre G, Thompson R, et al. Barth Syndrome. 2014 Oct 9 [Updated 2020 Jul 9]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK247162/.
3. Forzinity (elamipretide) [prescribing information]. Needham, MA: Stealth BioTherapeutics Inc.; September 2025.
4. Gwaltney C, Shields A, Love E, Ollis S, Stokes J, Mazar I, Arenson E, Aiudi A, Wirth RJ, Houts C. Initial Psychometric Evaluation of the Barth Syndrome Symptom Assessment (BTHS-SA) for Adolescents and Adults in a Phase 2 Clinical Study. Orphanet J Rare Dis. 2025 Apr 25;20(1):199. doi: 10.1186/s13023-025-03693-5.
5. Hornby B, Thompson WR, Almuqbil M, Manuel R, Abbruscato A, Carr J, Vernon HJ. Natural history comparison study to assess the efficacy of elamipretide in patients with Barth syndrome. Orphanet J Rare Dis. 2022 Sep 2;17(1):336. doi: 10.1186/s13023-022-02469-5.
6. Medline Plus .Barth syndrome. Available at: https://medlineplus.gov/genetics/condition/barth-syndrome/. Accessed November 14, 2025.
7. Reid Thompson W, Hornby B, Manuel R, Bradley E, Laux J, Carr J, Vernon HJ. A phase 2/3 randomized clinical trial followed by an open-label extension to evaluate the effectiveness of elamipretide in Barth syndrome, a genetic disorder of mitochondrial cardiolipin metabolism. Genet Med. 2021 Mar;23(3):471-478. doi: 10.1038/s41436-020-01006-8.
8. U.S. Food & Drug Administration. October 10, 2024: Meeting of the Cardiovascular and Renal Drugs Advisory Committee. Available at: https://www.fda.gov/advisory-committees/advisory-committee-calendar/october-10-2024-meeting-cardiovascular-and-renal-drugs-advisory-committee-10102024#event-materials. Accessed November 14, 2025.

Clinical Guideline Revision / History Information

Original Date: 02/02/2026
Reviewed/Revised: