VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Barth Syndrome – Forzinity Prior Authorization Policy
- Forzinity® (elamipretide subcutaneous injection)

REVIEW DATE: 12/09/2025

OVERVIEW

Forzinity, a mitochondrial protective agent, is indicated to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg.[1]

Forzinity was approved under accelerated approval based on an improvement in knee extensor muscle strength, an intermediate clinical endpoint.[1] Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Disease Overview

Barth syndrome is an ultra-rare, life-threatening, X-linked, infantile-onset, mitochondrial disorder characterized by cardiomyopathy, hypotonia, growth delay, neutropenia, and infections.[2] Currently, less than 250 patients have been diagnosed globally, but it is estimated that the disorder may be substantially underdiagnosed due to the variable clinical manifestation.[3] Barth syndrome is caused by mutations in the *TAZ* gene.[4] The *TAZ* gene is responsible for encoding the protein tafazzin. This protein is essential for the production of mature cardiolipin (CL), a mitochondrial-specific phospholipid. CL helps to maintain mitochondrial structure, energy production, and overall cellular function. Mutations in the TAZ gene lead to an abnormal CL composition. There is an accumulation of monolysocardiolipin ([MLCL] a precursor) and a deficiency of mature CL. Abnormal CL affects the structure and function of the inner mitochondrial membrane. Generally, tissues with the highest energy demands (e.g., heart and skeletal muscle) are most affected, leading to clinical features such as cardiomyopathy and muscle weakness. Additionally, mitochondrial dysfunction affects neutrophil activity, contributing to increased infection risk. The phenotype of Barth syndrome is variable but most frequently manifests as infantile-onset cardiomyopathy, myopathy, and neutropenia.[5] Additional features may include exercise intolerance, lactic acidosis, low serum and muscle carnitine, and increased organic acids in the serum or urine. A presumed diagnosis may be confirmed by molecular genetic analysis or by biochemical laboratory findings.[6] Biochemical findings include increased MLCL, decreased remodeled CL, and an abnormal MLCL/CL ratio in bloodspots, cells, and tissues.[7,8] Increased 3-methylglutaconic acid, 3-methylglutaric acid, and 2-ethylhydracrylic acid on urine organic acids analysis is also often seen.

Clinical Efficacy

In the pivotal study, patients were ≥ 12 years of age and weighed ≥ 30 kg with genetically confirmed disease.[9,10] Efficacy endpoints evaluated were the change from baseline in the six-minute walk test (6MWT), the total fatigue score (TFS), knee extensor muscle strength, 5 times sit-to-stand test (5xSST), and the SWAY balance score. During the randomized, double-blind component of the study (Part 1), a significant difference between Forzinity and placebo was not observed for any of the endpoints evaluated. In the open-label component of the pivotal study (Part 2), a significant improvement from baseline was observed through Week 168 in the 6MWT, muscle strength, and 5xSST; the mean TFS trended toward improvement from baseline at all measured timepoints through Week 168. Additionally, the effect of Forzinity on echocardiographic parameters or CL findings was evaluated to establish confirmatory evidence of clinical benefit. Of note, the reported 2D and 3D echocardiographic parameters at baseline were within the normal range in all patients. At the end of Part 1, there was no difference between Forzinity and placebo

in any of the echocardiographic parameters. Furthermore, subsequent changes reported in Part 2 were small, and generally still within the refence range of normal.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Forzinity. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Forzinity as well as the monitoring required for adverse events and long-term efficacy, approval requires Forzinity to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Forzinity is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Barth Syndrome.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** The patient weighs ≥ 30 kg; AND
     - **ii.** The diagnosis is established by ONE of the following (a, b, or c):
       - **a)** Patient has a laboratory test demonstrating an increased ratio of monolysocardiolipin (MLCL)/cardiolipin (CL) on erythrocytes, tissue, fibroblasts, or stored neonatal bloodspots; OR
       - **b)** Patient has a laboratory test demonstrating elevated 3-methylglutaric acid, 3-methylglutaconic acid (3-MGC), and 2-ethylhydracrylic acid on urine organic acids analysis; OR
       - **c)** Patient has a molecular genetic test demonstrating a hemizygous pathogenic variant in the tafazzin (*TAZ*) gene; AND
     - **iii.** The medication is prescribed by or in consultation with a geneticist, cardiologist, metabolic specialist, hematologist, pediatrician, or a physician who specializes in the treatment of mitochondrial disorders; OR
   - **B)** Patient is Currently Receiving Forzinity. Approve if the patients meets BOTH of the following (i and ii):
     - **i.** Patient has been established on therapy for at least 1 year; AND
       Note: A patient who has received < 1 year of therapy or who is restarting therapy with the requested drug should be considered under criterion A (Initial Therapy).
     - **ii.** According to the prescriber, the patient has demonstrated a clinical response, defined as stabilization or lack of decline from baseline (prior to initiating Forzinity).
       Note: Examples of a clinical response include stabilization or lack of decline in muscle strength, balance, six-minute walking distance, or fatigue.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Forzinity is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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7. Hornby B, Thompson WR, Almuqbil M, et al. 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 [Epub].
8. Ferreira C, Pierre G, Thompson R, et al. Barth Syndrome. 2014 Oct 9 [Updated 2020 Jul 9]. In: Adam MP, Bick S, 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/. Access on October 13, 2025.
9. Thompson WR, Hornby B, Manuel R, et al. 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;23(3):471-478.
10. Thompson WR, Manuel R, Abbruscato A, et al. Long-term efficacy and safety of elamipretide in patients with Barth syndrome: 168-week open-label extension results of TAZPOWER. *Genet Med.* 2024;26(7):101138.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/09/2025