

elamipretide (Forzinity™)

Policy # 00964

Original Effective Date: 05/01/2026

Current Effective Date: 05/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of elamipretide (Forzinity™)‡ to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of elamipretide (Forzinity) for indications other than to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg to be **investigational**.*

Background/Overview

Forzinity is a mitochondria-targeting peptide and the first FDA-approved therapy for Barth syndrome. It is approved to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg. Approval was granted under the FDA’s accelerated approval pathway based on improvements in knee extensor muscle strength, an intermediate clinical endpoint considered reasonably likely to predict clinical benefit. Continued approval depends on confirmation of clinical benefit in required post-marketing studies. Forzinity has received several FDA designations, including Orphan Drug, Fast Track, Priority Review, and Rare Pediatric Disease designation. These designations reflect the seriousness of Barth syndrome and the lack of previously approved treatment options.

Forzinity is designed to selectively localize to the inner mitochondrial membrane, where it binds cardiolipin, a key component of mitochondrial structure. Through this interaction, Forzinity is thought to help stabilize mitochondrial membranes, improve mitochondrial structure and function, increase cellular energy (ATP) production, and reduce oxidative stress. By targeting the underlying mitochondrial dysfunction caused by abnormal cardiolipin composition in Barth syndrome, Forzinity is intended to address a core disease mechanism that contributes to skeletal muscle weakness and reduced exercise capacity.

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For patients weighing at least 30 kg, the recommended dose of Forzinity is 40 mg administered subcutaneously once daily. The medication may be administered by the patient or a caregiver in the outpatient setting. Dose reduction is recommended in adults with severe renal impairment. Forzinity is supplied as single-patient-use vials and contains benzyl alcohol as a preservative; therefore, use is not recommended in neonates.

Barth Syndrome

Barth syndrome is an ultra-rare, X-linked mitochondrial disorder caused by pathogenic variants in the *TAZ* (tafazzin) gene, which is required for normal remodeling of cardiolipin. Cardiolipin plays an essential role in maintaining mitochondrial structure and energy production. When cardiolipin remodeling is impaired, mitochondrial function is disrupted, particularly in tissues with high energy needs, such as the heart and skeletal muscle. Clinical presentation varies, but commonly includes cardiomyopathy, skeletal muscle weakness, exercise intolerance, fatigue, hypotonia, growth delay, and neutropenia. Symptoms typically begin in infancy or early childhood. The highest risk of mortality occurs early in life, largely due to heart failure related to cardiomyopathy. Adolescents and adults often experience ongoing fatigue, limited stamina, and reduced physical functioning. There are currently no consensus treatment guidelines for Barth syndrome, and historically, management has focused on supportive and symptomatic care.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Forzinity is indicated to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg. The safety and effectiveness of Forzinity have not been established in pediatric patients weighing less than 30 kg.

This indication is approved under accelerated approval based on an improvement in knee extensor muscle strength, an intermediate clinical endpoint. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Forzinity was evaluated in a randomized, double-blind, placebo-controlled, crossover trial and its 192-week, open-label, single-arm extension period (TAZPOWER Part 1 and Part 2).

The randomized trial evaluated the efficacy and safety of once daily Forzinity 40 mg injected subcutaneously for 12 weeks in 12 subjects ≥ 12 -years-old and > 30 kg with genetically confirmed Barth syndrome. The primary endpoints for the randomized trial were distance walked during 6-minute walk test and Total Fatigue Score on the Barth syndrome Symptom Assessment. Forzinity was not superior to placebo on these primary endpoints. Ten subjects completed the randomized trial

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and entered the extension period designed to evaluate long-term safety and tolerability of Forzinity. Eight of these 10 subjects participated through Week 168 of the extension period. Knee extensor muscle strength measured by handheld dynamometry was evaluated as one of the secondary endpoints in the randomized trial and in the extension period. Increases in knee extensor muscle strength were not observed during the randomized trial but were observed during the extension period. At the pre-dose baseline visit at the start of the randomized trial, median muscle strength was 124 (92, 176) newtons. Significant improvements from baseline were observed for all patients on the mean muscle strength measured by hand-held dynamometry (HHD) at all visits with improvements ranging from 37.9 to 60.3 newtons ($P < 0.05$).

Although Forzinity received FDA accelerated approval based on improvement in knee extensor muscle strength measured by hand-held dynamometry, this outcome represents an intermediate surrogate endpoint rather than a direct measure of clinically meaningful benefit. The clinical relevance of this surrogate remains uncertain, and confirmatory evidence demonstrating sustained improvement in patient-centered or functional outcomes is lacking. Continued approval is contingent upon verification of clinical benefit in a post-marketing confirmatory trial, which has not yet been completed.

References

1. Forzinity [package insert]. Stealth Biotherapeutics, Inc. Needham, Massachusetts. September 2025.
2. Forzinity Drug Evaluation. Express Scripts. October 8, 2025.
3. Forzinity (elamipretide) New Drug Review, IPD Analytics. October 2025.

Policy History

Original Effective Date: 05/01/2026

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04/02/2026 Medical Policy Committee review

04/10/2026 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 04/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.