New Drug Overview

Forzinity (elamipretide)

PDL Category: Musculoskeletal Agents

Introduction

Disease Background:

- Mitochondria are organelles that generate energy for cellular processes. Furthermore, they are now involved in several facets of health and disease, such as cancer, aging, cardiovascular disorders, and nervous system disorders (*O'Ferrall 2026*).
  - Mitochondrial myopathies are primary mitochondrial diseases that manifest generally with muscle disease, and affect mainly or exclusively skeletal muscle. However, cardiac and/or smooth muscle may be involved in some cases.
    - The clinical phenotypes of mitochondrial myopathies are categorized as the following:
      - Isolated myopathy.
      - Chronic progressive external ophthalmoplegia (CPEO) or Kearns-Sayre syndrome (KSS).
      - Encephalomyopathy of infancy and childhood.
      - Multisystem disease with myopathy.
- Barth syndrome is a multi-organ mitochondrial disorder that affects muscle (*O'Ferrall 2026*).
  - It is a rare X-linked recessive genetic mitochondrial disorder due to mutations in the *tafazzin* gene, situated on the X chromosome (*Zhao et al 2025*).
    - When *tafazzin* does not work properly, it harms the synthesis of cardiolipin, which is a main phospholipid piece of the inner mitochondrial membrane. This results in decreased stability of the structure of the mitochondria and the electron transport chain, atypical mitochondrial energy metabolism, and the eventual beginning of symptoms such as cardiomyopathy, skeletal myopathy, delay in growth, neutropenia, and an increase in urinary excretion of 3-methyglutaconic acid (3-MGCA)
    - It is projected that the incidence of Barth syndrome is about 1 in 300,000 to 400,000 individuals.
- A multidisciplinary approach is needed to manage Barth syndrome to provide support of organ-specific manifestations (*Thompson et al 2022*).
- Forzinity was FDA approved in 2025.

Pharmacology/Usage

- Forzinity (elamipretide) is a mitochondrial cardiolipin binder. It localizes to the inner mitochondrial membrane and improves mitochondrial morphology and function.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Forzinity (elamipretide)
• To improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30kg. *	✔

***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.**

(Prescribing information: Forzinity 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

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Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Forzinity (elamipretide)	Solution for injection as single-patient-use vials: 280mg/3.5ml (80mg/ml)	SC	40mg subcutaneously (SC) once daily. -For use in patients weighing at least 30kg.	• Receive the dose at the same time each day. • If a dose is missed, skip the dose and take the next dose at the scheduled time. Do not take a double dose. • Adult patients or caregivers may administer Forzinity after proper training in preparing Forzinity vials for administration, if a healthcare provider determines that it is appropriate, and with medical follow-up as necessary. • Dose adjustment is not required with mild or moderate renal impairment. The dose should be reduced by one half in adults with severe renal impairment not on dialysis. Use has not been studied in patients with renal failure on dialysis.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Forzinity was assessed in a randomized, double-blind, placebo-controlled, crossover trial and its 192-week, open-label, single-arm extension period.
  - In the randomized trial, once daily Forzinity 40mg SC for 12 weeks in 12 subjects ≥12 years old and >30kg was compared with placebo in patients with generically 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.

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- Ten subjects completed the randomized trial and entered the extension period designed to assess 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 assessed 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 (min, max) muscle strength was 124 (92, 176) newtons.
      - The table below, adapted from the prescribing information, shows descriptive changes from pre-dose baseline for knee extensor muscle strength during the randomized controlled trial and extension period.

Table 3. Efficacy results

	Visit	N	Median Change	Min, Max Change
Randomized Controlled Trial	Week 12 placebo	12	-5	-31, 48
	Week 12 elamipretide	12	4	-41, 86
Open-Label Extension Period	Week 12	10	34	7, 95
	Week 24	9	68	3, 90
	Week 36	8	57	9, 92
	Week 48	8	41	-2, 144
	Week 72	8	35	-4, 100
	Week 168	8	63	38, 78

Clinical guidelines

- There are currently no published guidelines addressing the use of Forzinity.
- **Current and future treatment approaches for Barth syndrome** (*Thompson et al 2022*).
  - Current management of cardiomyopathy:
    - May need use of intravenous inotropes and diuretics for stabilization in infants with severe heart failure. ACE-inhibitors, beta-blockers and spironolactone may be appropriate oral medications.
    - Undergo routine electrocardiographic assessment to assist in monitoring QT interval and for arrhythmias.
  - Nutrition and growth:
    - Caloric intake and slow growth may be inadequate due to not being able to appropriately suck and swallow. Small, more frequent meals may be required to enable appropriate calorie intake.
    - Hypoglycemia has been reported.
    - Monitor growth regularly.
  - Neutropenia:
    - Reported in more than 80% with Barth syndrome and is the presenting clinical manifestation in about 18%.

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- Data suggests that over half with severe neutropenia have been reported to have major infections. The incidence has significantly decreased with the use of granulocyte colony stimulating factors.
- Fatigue, muscle weakness, and development:
  - These are significant clinical aspects of Barth syndrome.
  - Treatment goals are to optimize muscle function and balance fatigue, maximizing quality of life and being able to perform activities of daily living, educational and recreational activities, and work. Physical therapy is recommended.
- Genetic counseling is a key part of care.
- Elamipretide was not FDA approved prior to the publishing of this review, but it was discussed as therapy in ongoing clinical trials, as well as bezafibrate. Gene therapy and enzyme replacement therapy were also discussed.

Safety summary

- **Contraindications:**
  - Serious hypersensitivity to elamipretide or any of the excipients of the product.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Forzinity is not approved for use in neonates. Serious adverse reactions have been reported in low-birth weight neonates and preterm neonates who received benzyl alcohol (BA)-containing drugs intravenously. Forzinity is not approved for intravenous use.
    - The minimum amount of BA at which these serious adverse reactions, including fatal reactions, may occur is not known (Forzinity contains 20mg of BA per ml).
  - Hypersensitivity reactions, including serious allergic reactions requiring emergency medical intervention, have been reported in patients receiving Forzinity. These reactions have included skin manifestations such as rash, papular lesions, and eczematous dermatitis, as well as respiratory symptoms including cough. Reactions may occur within minutes to months after treatment initiation.
    - Monitor patients for signs and symptoms of hypersensitivity reactions during treatment. If a serious hypersensitivity reaction occurs, do not administer further doses of Forzinity and start appropriate emergency treatment, including epinephrine, antihistamines, and corticosteroids as clinically indicated. Patients who have experienced a serious hypersensitivity reaction should not be rechallenged with Forzinity.
    - For mild to moderate skin reactions, consider treatment with topical corticosteroids and oral antihistamines. Consider discontinuation of Forzinity if persistent or severe skin reactions develop.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (elamipretide) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included any local administration reaction (33%), injection site erythema (75%), injection site induration (50%), injection site pruritus (50%), injection site pain (33%), injection site bruising (25%), injection site urticaria (25%), and injection site hemorrhage (0%).

- **Drug interactions:** None.

- **Special populations:**

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- There is no pregnancy category for this medication; however, the risk summary indicates that Barth syndrome is not likely to affect females. Thus, there are no data with use in pregnant women to assess for a drug-related risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.
  - Forzinity contains benzyl alcohol as a preservative, which is rapidly metabolized by a pregnant women. Benzoyl alcohol exposure in the fetus is unlikely.
- The safety and efficacy of use have not been established in pediatric patients weighing less than 30kg.
  - Forzinity is not approved for use in neonates.

Conclusion

- Barth syndrome is a multi-organ mitochondrial disorder that affects muscle (*O'Ferrall 2026*).
  - It is a rare X-linked recessive genetic mitochondrial disorder due to mutations in the *tafazzin* gene, situated on the X chromosome (*Zhao et al 2025*).
- Forzinity is a mitochondrial cardiolipin binder indicated to improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30kg.
  - 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(s).
- The efficacy of Forzinity was assessed in a double-blind, placebo-controlled, crossover trial and its 192-week, open-label, single-arm extension period.
  - 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.
    - Knee extensor muscle strength measured by handheld dynamometry was assessed 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.
- There are no guidelines that have been published since FDA approval of Forzinity, but a review by Thompson et al in 2022 discussed elamipretide as being in ongoing clinical trials. Forzinity is, however, the first FDA approved treatment specifically for Barth syndrome.

- It is recommended that Forzinity should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.
- **PDL Placement:**

☐ Preferred
☒ Non-Preferred

References

- Forzinity. Package insert. Stealth Biotherapeutics Inc; September 2025.
- O'Ferrall EK. Mitochondrial myopathies: Clinical features and diagnosis. UpToDate website. Last updated April 27, 2026. Accessed June 15, 2026. https://www.uptodate.com.
- Thompson R, Jefferies J, Wang S, et al. Current and future treatment approaches for Barth syndrome. *J Inherit Metab Dis*. 2022; 45:17-28.
- Zhao C, Zhuang X, Gao J. Elamipretide: The first cardiolipin-directed mitochondrial therapeutic for Barth syndrome approved under accelerated approval. *Drug Discov Ther*. 2026; 19(6): 435-436.

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