

SS-31 FDA-approved for selected Barth syndrome patients

(Clinical studies: 40 mg daily SC. Community use: 5-40 mg daily SC)

SS-31 (elamipretide; MTP-131, Bendavia) is a synthetic aromatic–cationic tetrapeptide, D-Arg–2,6-dimethyl-Tyr–Lys–Phe-NH₂. SS-31 (elamipretide) targets mitochondrial cardiolipin. Laboratory research supports effects on membrane organization, electron transport, and oxidative stress; improved mitochondrial measurements have not necessarily translated into improved symptoms or physical function in trials. [5–7] The phase 3 primary mitochondrial myopathy trial was negative, while a small older-adult study found an acute bioenergetic signal without a significant prespecified functional benefit. General energy enhancement and human anti-aging benefits remain unproven. In September 2025, the FDA granted accelerated approval to improve muscle strength in adults and children with Barth syndrome weighing at least 30 kg, based on an intermediate muscle-strength endpoint; confirmatory clinical benefit remains to be verified. Results in other populations are mixed:. [1,2,4]

💉💉 Tolerability supported in studied populations. [1,3,12]

★ Effectiveness is likely for biomarker improvements, but only plausible for improvements to physical function. [1,2,4]

Disclaimer: These notes are not authoritative and should not be interpreted as definitive scientific guidance. They are summaries, compilations and plausible extrapolations drawn from the most relevant research I was able to locate, and may omit nuances, conflicting data, or emerging evidence. The material reflects an attempt to organize and understand complex topics, not to provide clinical recommendations or expert interpretation.



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Human tolerability is supported by controlled trials and a small Barth syndrome extension lasting over three years. Long-term evidence therefore exists, but its small, selected population limits conclusions about rare harms and routine use in otherwise healthy adults. [2,3,12]

Efficacy is indication-specific. MMPOWER-3 randomized 218 people with primary mitochondrial myopathy to 40 mg/day SC or placebo for 24 weeks. Neither six-minute walking distance nor total fatigue improved significantly versus placebo. This outweighs earlier exploratory signals for a broad PMM benefit, but does not prove absence of every biological effect in every population. [2]

Dosing & Patterns

Approved Barth syndrome regimen: 40 mg subcutaneously once daily for eligible patients. Adults with eGFR below 30 mL/min who are not on dialysis receive 20 mg daily; dosing is not

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established for dialysis or pediatric renal impairment. These are product-specific prescription doses. [1]

Research exposures: PROGRESS-HF tested 4 or 40 mg/day SC for 28 days without improving its primary cardiac endpoint. The older-adult study used a single two-hour IV infusion at 0.25 mg/kg/hour, not a daily low-dose SC regimen. [4,8]

SC bioavailability is approximately 92%, peak concentrations occur at 0.5–1 hour. [1] Daily SC treatment is the approved schedule, while research has also used single IV exposures and crossover washouts. MMPOWER-2 fatigue scores returned toward baseline after withdrawal; in older adults, the ATP-capacity difference was absent at day 7. Conversely, partial cardiac benefit persisted for weeks in old mice. These support that SS-31 effects last for a few days to a few weeks after completion of treatments rather than any lasting “repair effects.” [1,3,4,11]

Speculative community doses discussed are

- **5–40 mg/day, SC** - These are unvalidated community ranges, not established effective doses for energy, recovery, or longevity.

Benefits

- **Likely Improvement in muscle strength in Barth syndrome** — the approved indication is based on knee-extensor strength gains during open-label follow-up. The small randomized phase did not show superiority on walking distance or fatigue. (*Regulatory and human clinical evidence.*) [1,12,16]
- **Plausible Acute improvement in mitochondrial ATP-production capacity in selected older adults** — among 39 participants selected for low mitochondrial function, ATPmax increased 27% versus 12% with placebo. The percent-change comparison reached $P=0.045$, while the absolute-change comparison was $P=0.055$. But functional endpoints, coupling efficiency and the prespecified muscle-function analysis did not improve significantly. (*Small human trial; biomarker signal.*) [4]
- **Speculative Fatigue and exercise performance in primary mitochondrial myopathy** — MMPOWER-2 showed secondary patient-reported fatigue signals, but its primary walking-distance result was not significant. The larger MMPOWER-3 trial did not confirm walking or fatigue benefit. (*Mixed early evidence; negative phase 3 trial.*) [2,3]
- **Speculative reduction of oxidative stress and selected ischemic tissue injury** — liver and hind-limb experiments support protection in animal models, including changes in inflammation and autophagic flux. But, EMBRACE STEMI did not reduce its primary infarct-size biomarker endpoint. (*Animal and cellular evidence, with a negative human cardiac trial.*) [9,10,14]
- **Speculative mitochondrial respiration in failing human heart tissue** — demonstrated after direct ex vivo exposure, with no comparable effect in nonfailing samples. This supplies a plausible therapeutic mechanism, not proof of improved heart-failure outcomes after administration. (*Human tissue experiment.*) [7,8]

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- **Plausible improvement of selected age-related mitochondrial and cardiac deficits** — old-mouse experiments showed reduced mitochondrial oxidative stress and improved diastolic function and exercise performance. Human longevity or whole-body rejuvenation remains an extrapolation, not a demonstrated outcome. (*Animal evidence.*) [11]

Approved and Investigated Uses

- **Primary mitochondrial myopathy.** [2]
- **Barth syndrome.** [1,12,13,16]
- **Heart failure and reperfusion injury** Experimental. [8,14]
- **Retinal disease and aging** investigational. [11,15]

Cautions

- **Pregnancy and lactation:** Human data are insufficient; these are evidence gaps rather than blanket labeled contraindications. [1]
- **Renal impairment.** [1]
- **Unstable cardiac illness.** [1,8]

Side effects

- **Allergic reactions** — serious reactions are reported and may occur after early or prolonged exposure. [1]
- **Eosinophil increases** — reported during longer exposure, usually without associated clinical manifestations. [1]

Adverse effects can require discontinuation; tolerability is not equivalent to risk-free use. [2]

Diminished Response and Monitoring

Receptor desensitization is therefore not applicable. No evidence supports or rules out neutralizing antibodies, pathway adaptation, or whole-body compensation. [5,6]

Biological mechanism

Cardiolipin supports the organization of respiratory-chain proteins and mitochondrial cristae. SS-31 interacts with cardiolipin-containing membranes and the cardiolipin–cytochrome c complex; experiments show reduced peroxidase activity and improved electron transfer and ATP synthesis. This provides a plausible basis for reduced oxidative injury and improved cellular resilience, particularly in dysfunctional mitochondria. Human explanted-heart experiments support improved respiratory function, whereas the older-adult infusion study did not show improved resting ATP-to-oxygen coupling. Mechanistic effects should therefore be described by system and endpoint, not as universal restoration of mitochondrial efficiency. [4–7]

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Conclusions

SS-31 has a defined clinical role in Barth syndrome under accelerated approval, with small long-term follow-up supporting continued investigation. Broader claims of improved fatigue, exercise capacity, heart failure, or retinal disease must reflect the negative primary endpoints in the relevant controlled trials. [1–3,8,12,14–16]

The older-adult experiment supplies an acute bioenergetic signal, but without a noticeable energy boost. But, its negative prespecified functional analysis also does not prove that every person, dose, or longer treatment course must lack benefit. [4]

Lasting repair in healthy humans is unestablished. [3,4,11]

References

1. US Food and Drug Administration. Forzinity (elamipretide) injection: prescribing information. Revised September 2025. Accelerated approval; dosage, safety, pharmacology, and clinical studies. [Source](#)
2. Karaa A, Bertini E, Carelli V, et al. Efficacy and safety of elamipretide in individuals with primary mitochondrial myopathy: the MMPOWER-3 randomized clinical trial. *Neurology*. 2023;101(3):e238–e252. [doi:10.1212/WNL.000000000000207402](#)
3. Karaa A, Haas R, Goldstein A, Vockley J, Cohen BH. A randomized crossover trial of elamipretide in adults with primary mitochondrial myopathy. *J Cachexia Sarcopenia Muscle*. 2020;11(4):909–918. [doi:10.1002/jcsm.12559](#)
4. Roshanravan B, Liu SZ, Ali AS, et al. In vivo mitochondrial ATP production is improved in older adult skeletal muscle after a single dose of elamipretide in a randomized trial. *PLoS One*. 2021;16(7):e0253849. [doi:10.1371/journal.pone.0253849](#)
5. Szeto HH. First-in-class cardiolipin-protective compound as a therapeutic agent to restore mitochondrial bioenergetics. *Br J Pharmacol*. 2014;171(8):2029–2050. Mechanistic review. [doi:10.1111/bph.12461](#)
6. Birk AV, Chao WM, Bracken C, Warren JD, Szeto HH. Targeting mitochondrial cardiolipin and the cytochrome c/cardiolipin complex to promote electron transport and optimize mitochondrial ATP synthesis. *Br J Pharmacol*. 2014;171(8):2017–2028. Laboratory study. [doi:10.1111/bph.12468](#)
7. Chatfield KC, Sparagna GC, Chau S, et al. Elamipretide improves mitochondrial function in the failing human heart. *JACC Basic Transl Sci*. 2019;4(2):147–157. Ex vivo study. [doi:10.1016/j.jacbts.2018.12.005](#)
8. Butler J, Khan MS, Anker SD, et al. Effects of elamipretide on left ventricular function in patients with heart failure with reduced ejection fraction: the PROGRESS-HF phase 2 trial. *J Card Fail*. 2020;26(5):429–437. [doi:10.1016/j.cardfail.2020.02.001](#)
9. Shang L, Ren H, Wang S, et al. SS-31 protects liver from ischemia-reperfusion injury via modulating macrophage polarization. *Oxid Med Cell Longev*. 2021;2021:6662156. Animal and cellular study. [doi:10.1155/2021/6662156](#)

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10. Yang Q, Li C, Chen Q. SS31 ameliorates oxidative stress via the restoration of autophagic flux to protect aged mice from hind limb ischemia. *Front Cardiovasc Med*. 2022;9:789331. Animal and cellular study. [doi:10.3389/fcvm.2022.789331](https://doi.org/10.3389/fcvm.2022.789331)
11. Chiao YA, Zhang H, Sweetwyne M, et al. Late-life restoration of mitochondrial function reverses cardiac dysfunction in old mice. *eLife*. 2020;9:e55513. [doi:10.7554/eLife.55513](https://doi.org/10.7554/eLife.55513)
12. 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. Uncontrolled extension. [doi:10.1016/j.gim.2024.101138](https://doi.org/10.1016/j.gim.2024.101138)
13. ClinicalTrials.gov. A Trial to Evaluate Safety, Tolerability and Efficacy of Elamipretide in Subjects With Barth Syndrome (TAZPOWER). NCT03098797. Registry and protocol; results interpreted alongside publications. Accessed October 7, 2026. [Source](#)
14. Gibson CM, Giugliano RP, Kloner RA, et al. EMBRACE STEMI study: a Phase 2a trial to evaluate the safety, tolerability, and efficacy of intravenous MTP-131 on reperfusion injury in patients undergoing primary percutaneous coronary intervention. *Eur Heart J*. 2016;37(16):1296–1303. [doi:10.1093/eurheartj/ehv597](https://doi.org/10.1093/eurheartj/ehv597)
15. Ehlers JP, Hu A, Boyer D, et al. ReCLAIM-2: a randomized phase II clinical trial evaluating elamipretide in age-related macular degeneration, geographic atrophy growth, visual function, and ellipsoid zone preservation. *Ophthalmol Sci*. 2025;5(1):100628. Published online October 9, 2024. [doi:10.1016/j.xops.2024.100628](https://doi.org/10.1016/j.xops.2024.100628)
16. 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. [doi:10.1038/s41436-020-01006-8](https://doi.org/10.1038/s41436-020-01006-8)