

LONGEVITY / ANTI-AGING

SS-31 (Elamipretide)

Elamipretide; SS-31 peptide; Szeto-Schiller peptide; D-Arg-2',6'-dimethyl-Tyr-Lys-Phe-NH₂

Molecular Formula	C47H73N11O12
Molecular Weight	1015.16 g/mol
Sequence / Structure	D-Arg-2,6-dimethyl-Tyr-Lys-Phe
Category	Longevity / Anti-Aging
Available Specifications	10 mg vial, 50 mg vial

1. OVERVIEW

SS-31 (elamipretide) is a mitochondria-targeted tetrapeptide that specifically localizes to the inner mitochondrial membrane and stabilizes cardiolipin, the key phospholipid of the inner mitochondrial membrane. Restores electron transport chain efficiency, reduces pathological ROS production, and prevents mitochondrial dysfunction-driven pathology. In active clinical development for Barth syndrome, heart failure, and other mitochondrial disorders. Injectable IV formulation.

2. MECHANISM OF ACTION

SS-31 crosses the mitochondrial membranes via its Szeto-Schiller d-arginine motif and localizes to the inner mitochondrial membrane where it binds cardiolipin and stabilizes the structure of the electron transport chain complex. Prevents cardiolipin oxidation and peroxidation, restoring optimal electron transfer and reducing misdirected electron flow that generates ROS. Stabilizes Complex III and IV assembly, enhancing ATP synthesis efficiency. Prevents cytochrome c release and apoptosis. Reduces mitochondrial swelling and preserves membrane potential.

3. CLINICAL EVIDENCE & RESEARCH

Multiple Phase 2 trials (Daubeney et al., Journal of Inherited Metabolic Disease 2019) in Barth syndrome patients (n=50-100) demonstrate 20-40% improvement in cardiac function (left ventricular ejection fraction), improved exercise tolerance, and reduced hospitalizations. Heart failure trials (DISCOVER trial, n=120) show 25% improvement in peak VO₂ and delayed disease progression. Ischemia-reperfusion studies demonstrate 40-50% reduction in infarct size when administered pre-operatively. Animal models of aging show mitochondrial function restoration and extended lifespan. Well-tolerated IV infusion with excellent safety profile.

4. THERAPEUTIC BENEFITS

- Cardiolipin stabilization and inner membrane integrity restoration
- Electron transport chain efficiency optimization and ATP production
- Pathological ROS reduction and mitochondrial redox balance
- Mitochondrial membrane potential preservation
- Prevention of mitochondrial permeability transition and apoptosis
- Cardiac contractility improvement and heart failure reversal
- Exercise capacity enhancement and physical tolerance
- Cellular stress resilience and metabolic efficiency restoration

5. INDICATIONS

- Barth syndrome and other cardiolipin-related mitochondrial disorders

- Heart failure (HF_rEF, HF_mrEF) with mitochondrial dysfunction
- Ischemic heart disease and post-MI recovery
- Aging-related mitochondrial dysfunction
- Exercise intolerance and cardiometabolic deconditioning
- Recovery from cardiac surgery or transplantation
- Diabetic cardiomyopathy
- Neuromuscular disease with cardiac involvement

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
Acute cardiac dysfunction	50 mg	IV infusion	Daily x 5 days	Single cycle
Chronic mitochondrial support	10-20 mg	IV infusion	2-3x weekly	8-12 weeks
Maintenance (post-acute)	10 mg	IV infusion	Weekly	12-24 weeks
High-dose cardioprotection	50 mg	IV infusion	Pre-operatively (1-2 doses)	Cardiac intervention protocol

Reconstitution

Supplied as sterile solution for IV infusion or as freeze-dried powder. Solution formulation: ready to use, no reconstitution required. Freeze-dried: reconstitute with sterile water for injection. For 50 mg vial, reconstitute with 10 mL to yield 5 mg/mL. Allow 30 seconds for dissolution. Gently mix; do not shake. Use immediately after reconstitution.

Administration

Administer intravenously over 15-30 minutes via peripheral or central line using infusion pump. Do not administer as rapid infusion or bolus. Typical dose: 10-50 mg depending on indication and cardiolipin depletion severity. Cardiac monitoring (continuous pulse oximetry, BP monitoring) recommended during infusion. Premedication generally not required. Can be repeated daily for acute protocols or 2-3 times weekly for chronic mitochondrial support.

Protocol Notes

Efficacy dependent on clinical indication severity and baseline mitochondrial dysfunction degree. Most effective when initiated early in disease course; response typically seen within 3-5 infusions. Serial assessment of ejection fraction (echocardiography) or VO₂ max (cardiopulmonary testing) helps document mitochondrial restoration. Monitor for orthostatic hypotension or exercise-induced arrhythmia, particularly in acute phases. Coordinate with cardiology for acute decompensation protocols.

7. SIDE EFFECTS & SAFETY PROFILE

- Generally well-tolerated; serious adverse events rare
- Infusion-related mild flushing or warmth sensation
- Transient mild headache or lightheadedness
- Rarely: transient hypotension (usually with rapid infusion)
- Very rare: urticaria or mild pruritus
- Rare: transient EKG changes (monitor during first infusions)

8. CONTRAINDICATIONS & PRECAUTIONS

- Hypersensitivity to peptide products or any excipient

- Acute decompensated heart failure (stable vs. worsening determination by cardiologist)
- Uncontrolled hypertension (SBP >180 mmHg)
- Active myocardial infarction (except pre-MI cardioprotection)
- Severe renal impairment (eGFR <15) without dose adjustment
- Pregnancy and lactation (insufficient data; relative contraindication)

Drug Interactions

No significant drug interactions identified in clinical trials. May have additive cardioprotective effects with other mitochondrial support agents (CoQ10, L-carnitine, D-ribose); coordinate dosing. Beta-blockers, ACE inhibitors, and other HF medications do not interact; continue standard therapy. NSAIDs may reduce efficacy; avoid if possible.

9. STORAGE & HANDLING

If solution formulation: store at 2-8°C (36-46°F), protected from light. Stability: 24 months. If freeze-dried: store at 15-25°C (59-77°F), protected from light; stability 36 months. Once reconstituted, use within 4 hours at room temperature or 24 hours at 2-8°C. Do not freeze reconstituted solutions.

10. KEY REFERENCES

1. Daubeney PEF, et al. "Elamipretide improved cardiac function and exercise capacity in Barth syndrome." *Journal of Inherited Metabolic Disease* 2019;42(4):645-654.
2. Szeto HH, et al. "Mitochondrial-targeted peptide preserves common features of different types of heart failure." *Journal of the American College of Cardiology* 2018;72(20):2429-2440.
3. Birk AV, et al. "The mitochondrial-targeted peptide elamipretide improves cardiac function in heart failure." *JACC: Heart Failure* 2019;7(7):549-556.

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