

RESEARCH MONOGRAPH . COMPOUND PROFILE

Melanotan I (Afamelanotide)

*A linear alpha-MSH analog approved as
Scenesse for erythropoietic
protoporphyrria, characterized by
sustained skin pigmentation.*

DOCUMENT	KDC-MN-092
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COMPOUND CLASS	Alpha-MSH analog (linear heptadecapeptide)

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ABSTRACT

Melanotan I (Afamelanotide, Scenesse; (Nle⁴, D-Phe⁷)-alpha-MSH; CAS 75921-69-6; molecular formula C₇₈H₁₁₁N₂₁O₁₉; molecular weight 1646.85) is a linear heptadecapeptide analog of alpha-melanocyte stimulating hormone (alpha-MSH) developed at the University of Arizona by Mac Hadley's group in the 1980s. The compound was approved by the FDA in 2019 (and earlier in Europe) for erythropoietic protoporphyria, a rare genetic photosensitivity disorder. Mechanism is non-selective melanocortin receptor agonism (MC1, MC3, MC4, MC5); the MC1 activity drives melanin synthesis in melanocytes producing tan-like skin pigmentation. The clinical formulation is a 16 mg subcutaneous implant providing sustained release over 60 days. The compound is sold as a research chemical/peptide for sunless tanning applications, though regulatory authorities have issued warnings against this use. Pharmacokinetics: subcutaneous administration; the implant formulation provides 30 to 60 days of activity per dose.

1. Compound Identification

Melanotan I (Afamelanotide) is described as alpha-msh analog (linear heptadecapeptide). A linear alpha-MSH analog approved as Scenesse for erythropoietic protoporphyria, characterized by sustained skin pigmentation.

1.1 Class summary

Alpha-MSH analog (linear heptadecapeptide)

1.2 Subtitle

A linear alpha-MSH analog approved as Scenesse for erythropoietic protoporphyria, characterized by sustained skin pigmentation.

2. Abstract

Melanotan I (Afamelanotide, Scenesse; (Nle4, D-Phe7)-alpha-MSH; CAS 75921-69-6; molecular formula C₇₈H₁₁₁N₂₁O₁₉; molecular weight 1646.85) is a linear heptadecapeptide analog of alpha-melanocyte stimulating hormone (alpha-MSH) developed at the University of Arizona by Mac Hadley's group in the 1980s. The compound was approved by the FDA in 2019 (and earlier in Europe) for erythropoietic protoporphyria, a rare genetic photosensitivity disorder. Mechanism is non-selective melanocortin receptor agonism (MC1, MC3, MC4, MC5); the MC1 activity drives melanin synthesis in melanocytes producing tan-like skin pigmentation. The clinical formulation is a 16 mg subcutaneous implant providing sustained release over 60 days. The compound is sold as a research chemical/peptide for sunless tanning applications, though regulatory authorities have issued warnings against this use. Pharmacokinetics: subcutaneous administration; the implant formulation provides 30 to 60 days of activity per dose.

3. Mechanism of Action

Non-selective melanocortin receptor agonist (MC1-MC5). MC1 activity drives skin pigmentation.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

16 mg implant every 60 days (clinical use).

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Langendonk JG, et al. Afamelanotide for erythropoietic protoporphyria. N Engl J Med 2015.

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