

5 Amino 1MQ

For Body Recomp 100–200 mg daily for several weeks, For healthspan 25–50 mg daily

5-Amino-1MQ has demonstrated adipose, metabolic, and aged-muscle effects in specific animal models. [2,4,7–9,17] 5-Amino-1MQ (5-amino-1-methylquinolinium) is an experimental small-molecule inhibitor of nicotinamide N-methyltransferase (NNMT). [1,2] Reduced adiposity has been observed in obese-mouse experiments. [2,4] Higher NAD⁺ was reported in cultured adipocytes and, separately, mouse muscle after NNMTi treatment. [2,17] Mitochondrial and epigenetic consequences remain context-dependent. [3,13,18]

❓ Human safety unestablished; preclinical findings differ by endpoint

★ Plausibly effective for body recomposition

★ Plausible selected healthspan benefits; lifespan extension speculative

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.

Human pharmacokinetics, efficacy, and safety remain unestablished. [2,7–9,12,13,17]

Evidence Summary

The strongest direct evidence concerns selected endpoints in obese or aged mice. The diet-combination and microbiome studies are related, condition-specific experiments. [4,5] Several foundational studies share investigators and disclose commercial interests. [4,7–9] Independent studies extend the muscle evidence, but reproduce different models and endpoints rather than all earlier findings. [16,17] Human translation remains untested. Findings with JBSNF-000088 and newer inhibitor chemotypes provide target-level context, not compound-specific efficacy. [6,11]

Animal Pharmacokinetics and Human Mechanistic Extrapolations

Animal pharmacokinetic data are available for 5-Amino-1MQ, including oral, intravenous (IV), and subcutaneous (SC) administration. No human PK data have been established. The animal studies show substantial differences between species and routes of administration, particularly for oral bioavailability. [7,10]

HEDs below are expressed as active 5-amino-1-methylquinolinium, excluding the counterion. [1,2] They are experimental comparisons, not established human doses. [14]

Animal Regimen

Mouse IV — PK [7]

Mouse SC — PK [7]

Human Equivalent Dose (150 lbs) [14]

~15 mg once

~77 mg once; or daily for 5 days

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Animal Regimen

Mouse SC — weight/adipose loss [2]
Mouse SC — body composition [4]
Mouse SC — metabolic outcomes [7]
Mouse SC — aged muscle function [8]
Mouse SC — injury regeneration [9]
Mouse IP — limb function [16]
Mouse IP — aged muscle function [17]
Mouse IP — D-gal muscle function [17]
Mouse IP — cardiac function [18]
Mouse IP — bladder tumor [19]

Human Equivalent Dose (150 lbs) [14]

~62 mg three times daily for 11 days
~98 mg daily for 7 weeks
~31 or 98 mg daily for ~4 weeks
~31 mg daily for 8 weeks
~15 or 31 mg twice daily around injury
~31 mg daily
~61 mg daily for 5 weeks
~15 or 31 mg daily
~15 mg twice daily for 3 days
~31 mg every 12 hours

Body Recomposition Dosing Patterns

In obese mice, approximately 62 mg HED SC three times daily for 11 days produced weight and adipose-mass loss. [2,14] A later diet-combination experiment used approximately 98 mg HED SC daily for seven weeks and improved body composition. [4] In a separate approximately four-week study, approximately 98 mg HED SC daily limited body-weight and fat-mass gain, whereas approximately 31 mg HED SC daily did not; some biochemical outcomes changed at the lower dose. These findings must not all be described as weight loss. [7]

The speculative, experimental daily SC body-recomposition dose is

- **100-200 mg daily for several weeks**

Healthspan Dosing Patterns

A directly relevant aged-mouse experiment used approximately 31 mg HED SC daily for eight weeks in females aged 22–24 months. Grip strength improved, including with exercise, but plantarflexor peak torque did not significantly improve and cumulative work was lower in treated groups. Benefits were endpoint-specific. [8,14] The injury study used approximately 15 or 31 mg HED SC twice daily around induced muscle injury, supporting regeneration rather than general healthspan. [9] Independent work also tested approximately 61 mg HED IP daily for five weeks in naturally aged females and approximately 15 or 31 mg HED IP daily in a D-galactose model. [17]

The speculative, experimental daily SC healthspan dose is

- **25–50 mg daily**

Repeated dosing over weeks has been studied, but the identified experiments do not establish a lifelong regimen, very-low-dose continuous exposure, or optimal healthspan cycles. Continuous treatment and intermittent schedules remain competing research hypotheses. [7–9,17]

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Continuous NNMT Inhibition and Long-term Safety

Repeated exposure over weeks provides limited preclinical tolerability information, including eight weeks in old mice, but the muscle study was not a comprehensive chronic-toxicology program. [8] Improvements in selected metabolic and liver endpoints offer more specific reassurance in obese mice. [4,7]

Reducing NNMT activity may preserve nicotinamide for NAD⁺ salvage and conserve SAM, with consequences that differ by tissue. [2,3,13] NNMT/1-MNA signaling also protected against hepatic ischemia–reperfusion injury, while uterine NNMT deficiency impaired implantation-related biology. [12,13] These results make loss of beneficial NNMT functions a biologically supported concern, but do not demonstrate chronic toxicity from 5-Amino-1MQ. Partial or intermittent inhibition is a defensible hypothesis for balancing effects, but existing studies do not establish it as safer than other schedules.

Whether lower daily exposure, intermittent inhibition, or treatment cycles provide the best balance of benefit and safety remains unknown.

Plausible Benefits

- **Adiposity and fat mass:** compound-specific mouse studies support an effect on adipose biology. [2,4]
- **NAD⁺ and energy metabolism:** cell experiments and NNMT knockdown studies support links to NAD⁺ salvage, SAM availability, and energy metabolism. Genetic target manipulation is not equivalent to administering 5-Amino-1MQ. [2,3]
- **Glucose regulation:** improved glucose handling and reduced hyperinsulinemia were reported in diet-induced obese mice. [7]
- **Muscle regeneration and function:** aged-mouse studies reported improved injury recovery and selected functional outcomes, including grip strength; effects vary by muscle and test. [8,9,17]
- **Obesity-associated hepatic steatosis:** improvements have been reported in mouse disease models, including in combination with dietary change. [4,7]

Potential Applications

- **Obesity and adiposity reduction:** investigational indication supported by mouse experiments. [2,4]
- **Metabolic dysfunction and age-related muscle impairment:** research indications with convergent preclinical rationale; human efficacy remains plausible rather than established. [7–9,17]

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Cautions

- **Pregnancy, conception, and breastfeeding:** compound-specific safety is unestablished. A 2026 study associated NNMT deficiency with impaired endometrial decidualization and found fewer implantation sites after uterine NNMT knockdown in mice. This is target-level reproductive concern, not reproductive toxicology of 5-Amino-1MQ. [13]
- **Hepatic and renal impairment:** human clearance and dose adjustments are unknown.
- **Drug interactions:** no human interaction profile was identified. An in vitro off-target MAO-A signal warrants investigation, but does not establish clinically meaningful MAO inhibition or a specific drug interaction at human exposures. [7] Altered nicotinamide and methyl-donor metabolism provides additional mechanistic hypotheses. [3,13]

Reported or Possible Side Effects

- **Altered methyl-donor metabolites:** a mechanistic possibility rather than a demonstrated human adverse effect. Direction and clinical significance may differ across tissues. [3,13]

Drivers of Diminished Response and Mitigation Strategies

Whether responses diminish with sustained treatment is unestablished. Changes in downstream pathways are hypotheses for altered response. Its effects on nicotinamide and methyl-donor metabolism provide biological context for such hypotheses. [2,3]

Endpoint-specific Safety Evidence and Unresolved Risks

None of the safety domains below has established human tolerability at a defined dose or duration. The distinctions below reflect observed preclinical results and the limits of longer-term inference.

- **Hepatic:** reduced steatosis or improved liver biochemistry in obese mice provides endpoint-specific reassurance over weeks. [4,7] In a different ischemia–reperfusion context, NNMT/1-MNA was protective; the inhibitor arm used JBSNF-000088, not 5-Amino-1MQ. [12] These findings support possible hepatic benefit in selected disease settings, but do not establish broadly favorable long-term human hepatic safety.
- **Endocrine, metabolic, and reproductive:** glucose regulation and hyperinsulinemia improved in obese mice, supporting plausible metabolic benefit. [7] NNMT manipulation also changes SAM/SAH and methylation biology. [3,13] Endometrial findings identify a specific reproductive concern; compound-specific fertility, pregnancy, developmental, and lactation risks remain insufficiently characterized. [13]
- **Renal and NAD⁺ biology:** 5-Amino-1MQ reduced injury-associated signatures in cultured tubular cells and kidney organoids, providing a renal therapeutic hypothesis rather than chronic renal safety evidence. The animal inhibitor arm used RT001 and should not be

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attributed to 5-Amino-1MQ. [15] NAD⁺ responses depend on biological context; pathway effects in one tissue cannot establish whole-body healthspan benefit. [2,3,15,18]

- **Immunological:** lower circulating white-cell subsets in obese mice were interpreted as reduced obesity-associated inflammation. [7] Reduced inflammatory cytokines in cultured human orbital fibroblasts provide additional mechanistic evidence. [20]
- **Proliferative and carcinogenic:** tumor inhibition in a bladder-cancer mouse model is encouraging in that setting, but cannot exclude delayed cancer risk or establish safety of lifelong use. [19]

Healthspan Benefits and Rationale

The 2019 injury study and 2024 aged-muscle study measured regeneration and function. In the latter, mice aged 22 to 24 months received approximately 31 mg HED subcutaneously daily for eight weeks; grip strength improved and treatment plus exercise produced additional benefit. Effects were endpoint-specific and do not demonstrate reversal of aging. [8,9]

Preclinical justification: Preserving selected muscle functions and reducing pathological adiposity could plausibly improve aspects of human healthspan. [2,4,8,9,17] This is a translational inference, limited by disease-model relevance, endpoint differences, and unknown human exposure; the available evidence does not justify upgrading it to likely benefit in healthy adults.

Chanvillard et al. linked NNMT to tubular senescence and fibrosis in human kidney specimens and tested 5-amino-1-methylquinolinium in tubular cells and human kidney organoids. The animal pharmacological arm used RT001. These findings support a kidney-specific hypothesis, not generalized senolysis or demonstrated healthspan extension. [15]

Dong et al. used NNMTi (HY-131042) at approximately 31 mg HED IP daily in a mouse hindlimb-ischemia model. Strength, power, and work improved without improved perfusion or capillary density. [16] Liang et al. separately reported selected functional improvements in aged and D-galactose-treated mice, with increased muscle NAD⁺ and AMPK/PGC1 α markers. Not all muscle contraction endpoints improved. [17]

NAD⁺ salvage and methyl-donor conservation offer hypotheses for metabolic resilience without establishing that persistent NNMT suppression improves aging. [2,3,17] Results involving newer chemotypes are target-level evidence and cannot be counted as direct 5-Amino-1MQ efficacy. [11] Compound-specific antitumor effects in mice similarly do not establish general healthspan or lifespan benefit. [19]

However, NNMT and 1-MNA can have beneficial functions in particular tissues or stress states. Recent liver and reproductive findings argue against treating NNMT as uniformly harmful. A

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healthspan claim, even just plausible healthspan improvement claims, requires consideration of NNMT benefits and these tradeoffs. [12,13]

Biological mechanism

NNMT transfers a methyl group from S-adenosylmethionine (SAM) to nicotinamide (NAM), producing 1-methylnicotinamide (1-MNA) and S-adenosylhomocysteine (SAH). [1–3] Inhibition can preserve NAM for NAD⁺ salvage and change methyl-donor flux. [2,3] 5-Amino-1MQ inhibits NNMT in biochemical and cellular assays, with low-micromolar potency in early work. [1,2] Connections to sirtuins, polyamine flux, epigenetic state, and energy metabolism are supported to varying degrees by cell, genetic, and pharmacological studies; they are not a fully demonstrated causal chain in humans. [2,3]

Conclusions

5-Amino-1MQ is a preclinical research compound with a rationale for studying metabolic disease and selected muscle dysfunction. Human body-recomposition and selected healthspan benefits are plausible extrapolations; healthspan extension remains speculative. [2,4,7–9,17] Animal HEDs do not establish human dosing. [14] Safety must be assessed by endpoint and exposure duration. [7,12,13,18–20]

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