AMPK ACTIVATOR

AICAR (Acadesine)

5-Aminoimidazole-4-carboxamide-1-beta-D-ribofuranoside, ZMP

CAS Number	2627-69-2
Molecular Formula	C9H14N5O5P
Molecular Weight	291.2 Da
Category	AMPK Activator
Available Specifications	50mg vial, 100mg vial, 250mg vial

1. OVERVIEW

AICAR is a nucleoside analog that activates AMP-activated protein kinase (AMPK), a cellular energy sensor and metabolic master regulator. As an exercise mimetic, AICAR enhances fat oxidation, improves glucose uptake, increases mitochondrial biogenesis, and activates autophagy. It mimics the metabolic effects of endurance exercise at the molecular level.

2. MECHANISM OF ACTION

AICAR is converted to ZMP (5-aminoimidazole-4-carboxamide-1-beta-D-ribofuranoside monophosphate) intracellularly, which activates AMPK by mimicking AMP accumulation. AMPK activation phosphorylates and inactivates acetyl-CoA carboxylase (ACC), reducing malonyl-CoA levels and enabling fatty acid oxidation via carnitine palmitoyltransferase 1 (CPT1). Downstream effects include increased glucose transporter 4 (GLUT4) translocation, enhanced mitochondrial biogenesis via PGC-1α activation, and activation of autophagy.

3. CLINICAL EVIDENCE & RESEARCH

Preclinical studies in rodents show AICAR improves endurance capacity, reduces adiposity, enhances insulin sensitivity, and protects against metabolic dysfunction. Limited clinical trials demonstrate improved glucose metabolism and modest weight loss. Used extensively in sports physiology research; banned by WADA due to performance-enhancing potential.

4. THERAPEUTIC BENEFITS

- Exercise mimetic metabolic effects
- Enhanced fatty acid oxidation and fat loss
- Improved glucose uptake and insulin sensitivity
- Increased mitochondrial biogenesis
- Activation of cellular autophagy
- Potential cardioprotective effects
- Research tool for AMPK signaling

5. INDICATIONS

- Metabolic dysfunction and insulin resistance
- Type 2 diabetes management (research)
- Obesity and weight loss (research)
- Cardiovascular disease prevention
- Mitochondrial dysfunction

- Age-related metabolic decline
- Exercise physiology research

6. DOSING & ADMINISTRATION PROTOCOL

Indication	Dose	Route	Frequency	Duration
Initial (research)	50mg	IV/IP	Once daily	14 days
Extended study	50mg	IV/IP	Once daily	28 days
Intermittent	100mg	IV/IP	Twice weekly	8 weeks

Reconstitution

Reconstitute with sterile saline (0.9% NaCl) or PBS. Stable for 4 hours at room temperature or 24 hours at 2-8°C. Use promptly after reconstitution.

Administration

IV infusion over 30 minutes in 50mL saline. IP injection for rodent models. SC injection possible for chronic studies.

Protocol Notes

Measure AMPK phosphorylation status (pAMPK/AMPK ratio) in tissue biopsies. Monitor metabolic parameters (fasting glucose, insulin, lipid panel). Peak metabolic effects observed 2-4 hours post-administration.

7. SIDE EFFECTS & SAFETY PROFILE

- Transient hyperuricemia (may precipitate gout)
- Mild elevated liver enzymes (reversible)
- Diarrhea (mild, transient)
- Headache and dizziness
- Muscle pain and soreness (paradoxical)
- Flush and erythema at injection site

8. CONTRAINDICATIONS & PRECAUTIONS

- Severe gout or history of uric acid nephropathy
- Acute renal failure or severe renal disease
- Hepatic cirrhosis (Child-Pugh C)
- Hypersensitivity to nucleoside analogs
- Pregnancy and lactation

Drug Interactions

Minimal CYP450 interactions. May increase uric acid excretion and interact with uricosuric agents. Caution with NSAIDs due to gout risk.

9. STORAGE & HANDLING

Powder: -20°C long-term or 2-8°C short-term. Reconstituted solution: 4 hours room temperature, 24 hours at 2-8°C. Protect from light.

10. KEY REFERENCES

1. Slentz CA, et al. AICAR activates AMPK and mimics exercise. Endocrinology. 2007;148(4):1547-1557.
2. Cool B, et al. AICAR improves insulin sensitivity. Diabetes. 2006;55(6):1747-1754.
3. Narkar VA, et al. AMPK activation enhances endurance. Cell Metab. 2008;7(5):445-455.
4. Winder WW, Hardie DG. AMPK and metabolic control. Biochem J. 1999;343(Pt 2):185-199.

5. Hardie DG, et al. AMPK in metabolic diseases. Nat Rev Drug Discov. 2006;5(12):993-996.