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## S-ADENOSYL-L-METHIONINE (SAME) Fact Sheet [G]

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### Bottom Line:

SAME is a natural methyl donor important in neurotransmitter synthesis and function. Several clinical studies (lasting up to 42 days) have shown that taking SAME is more effective than placebo and appears to be as effective as tricyclic antidepressants, though the studies were limited in various ways. Consider using it for those patients with mild to moderate depression who are interested in using alternative therapies, or as an augmentation strategy in partial responders.

### FDA Indications:

None.

### Off-Label Uses:

Depression; osteoarthritis; cirrhosis and fatty liver disease.

### Dosage Forms:

Supplied over the counter most often as 100 mg, 200 mg, 400 mg tablets, usually enteric coated.

### Dosage Guidance:

Effective dose is variable, but most antidepressant studies have used doses of about 400–1600 mg/day (1600 mg most common), usually divided BID.

**Monitoring:** No routine monitoring recommended unless clinical picture warrants.

**Cost:** \$

### Side Effects:

- Most common: Well tolerated. Higher doses may result in flatulence, nausea, vomiting, diarrhea, constipation, dry mouth, headache, mild insomnia, anorexia, sweating, dizziness, and nervousness. Anxiety and tiredness have occurred in people with depression, and hypomania has occurred in people with bipolar disorder.
- Serious but rare: Theoretical concern of elevated homocysteine since SAME is converted to this during normal metabolism. No reports to date, but some recommend taking folate and vitamin B supplements anyway.
- Pregnancy/breastfeeding: Not enough data to recommend.

### Mechanism, Pharmacokinetics, and Drug Interactions:

- Methyl group donor that may increase synthesis of neurotransmitters, increase responsiveness of neurotransmitter receptors, and increase fluidity of cell membranes through the production of phospholipids.
- Metabolism similar to endogenous SAME (transmethylation, trans-sulphuration, and aminopropylation);  $t_{1/2}$ : 100 minutes.
- No drug interactions reported. Theoretically, serotonin syndrome possible but risk likely minimal.

### Clinical Pearls:

- SAME is produced by our bodies as a derivative of the amino acid methionine. It is necessary for the production of serotonin and norepinephrine (and in more than 100 other biochemical reactions) throughout virtually all body tissues and fluids. Concentrations are highest in childhood and decrease with age.
- SAME is difficult to formulate as a stable oral salt, and the FDA halted trials of an investigational prescription product in 1993 due to concerns about tablet dissolution; concerns have been raised that some supplements may also have these problems.

### Fun Facts:

SAME has been available as a dietary supplement in the US since 1999, but it has been used as a prescription drug in Italy since 1979, in Spain since 1985, and in Germany since 1989. Patients in trials of SAME for depression noted improvement in their arthritis symptoms, suggesting another possible use.