



SAMe

Natural Standard Bottom Line Monograph, Copyright © 2010 (www.naturalstandard.com). Commercial distribution prohibited. This monograph is intended for informational purposes only, and should not be interpreted as specific medical advice. You should consult with a qualified healthcare provider before making decisions about therapies and/or health conditions.

While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

Related Terms:

- Ademetionin, ademetionine, adenosylmethionine, Ade-SD4, AdoMet, Geptral (Russian), Gumbaral (German), Heptral (Russian), S-adenosylmethionine, SAM-e, Sammy, Samyr (Italian), sulfoadenosilmethionina (Italian), sulfo-adenosil-L-metionina (Spanish), sulfo-adenosyl-L-methionine sulfate-p-toluensulfonate (stable salt form), sulfo-adenosyl-methionine.

BACKGROUND

- SAME was first discovered in 1953 by a researcher named Cantoni. It is formed in the body from methionine and adenosine triphosphate in a reaction catalyzed by methionine adenosyltransferase. SAME functions as a primary methyl group donor in a variety of reactions in the body. After donating a methyl group, SAME is converted to S-adenosyl-homocysteine.
- SAME is used for psychiatric illnesses, infertility, liver concerns, premenstrual disorders and musculoskeletal disorders, among others.
- SAME has been studied extensively in the treatment of osteoarthritis and depression. Many trials provide evidence that SAME reduces the pain associated with osteoarthritis and is well tolerated in this patient population. Some evidence is available for the use of SAME for intrahepatic cholestasis of pregnancy although additional study is needed in this area. Anti-inflammatory and analgesic (pain relieving) activity has also been attributed to SAME.
- Future well-designed clinical trials are required in the areas of depression, fibromyalgia and liver cholestasis before a strong recommendation can be made in these areas.

SCIENTIFIC EVIDENCE

Uses

These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.

Grade*

<p>Osteoarthritis</p> <p>SAMe has been studied extensively in the treatment of osteoarthritis. SAMe reduces the pain associated with osteoarthritis and is well tolerated in this patient population. Although an optimal dose has yet to be determined, SAMe appears as effective as the non-steroidal anti-inflammatory drugs (NSAIDs). Additional study is warranted to confirm these findings.</p>	<p><u>B</u></p>
<p>Attention deficit hyperactivity disorder (ADHD)</p> <p>Preliminary evidence from an open trial suggests that SAMe may be of benefit for adults with ADHD. More study is needed in this area.</p>	<p><u>C</u></p>
<p>Cholestasis (pregnancy)</p> <p>Currently, there is insufficient available evidence to recommend for or against the use of SAMe for cholestasis (build up of bile in the liver) in pregnant women. It is important to note that there is no information on the use of SAMe prior to the third trimester.</p>	<p><u>C</u></p>
<p>Cholestasis (non-pregnant)</p> <p>SAMe may be beneficial for pruritus (severe itching) and serum bilirubin levels associated with cholestasis associated with non-pregnancy. However, additional study is needed.</p>	<p><u>C</u></p>
<p>Depression</p> <p>SAMe has been studied for use in depression for many decades, however, currently available trials are inconclusive.</p>	<p><u>C</u></p>
<p>Fibromyalgia</p> <p>Since fibromyalgia is characterized by chronic pain and depressive symptoms, there is an increased interest in studying SAMe for this indication. Current available evidence, however, does not appear to show any benefit of SAMe over placebo in reducing the number of tender points and in alleviating depression. Additional study is needed to confirm these findings.</p>	<p><u>C</u></p>
<p>Liver disease (general)</p> <p>Preliminary evidence suggests that SAMe may normalize levels of liver enzymes in individuals with liver disease. Additional study is needed in this area.</p>	<p><u>C</u></p>

***Key to grades:** **A:** Strong scientific evidence for this use; **B:** Good scientific evidence for this use; **C:** Unclear scientific evidence for this use; **D:** Fair scientific evidence against this use (it may not work); **F:** Strong scientific evidence against this use (it likely does not work).

TRADITION/THEORY

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- Acetaminophen metabolism (hepatic cirrhosis), adjustment disorder, aging, alcoholism, Alzheimer's disease, anxiety, bilirubin and polyphyrin metabolism disorders, bursitis, cirrhosis (primary biliary), dementia, bipolar disorder, drug/toxin induced hepatotoxicity (liver damage), gastritis (hemorrhagic), Gilbert's syndrome, heart disease, hepatitis, high cholesterol, infertility, intrahepatic cholestasis (oral-contraceptive-induced), intrahepatic cholestasis (total parenteral nutrition-induced), ischemic stroke, lead toxicity, male sterility, migraine, multiple sclerosis, pancreatitis, myelopathy (spinal cord injury), Parkinson's disease, post-concussive syndrome, postpartum depression, premenstrual syndrome, premenstrual dysphoric disorder, psychiatric illness, rheumatoid arthritis, seizures, Sjogren's syndrome, systemic sclerosis, tendonitis.

DOSING

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older):

- Both oral (taken by mouth) and intravenous (injection) preparations of SAME have been studied in clinical trials with some evidence of benefit for certain conditions. SAME appears effective for osteoarthritis, and 600-1,200 milligrams has been taken daily in 1-3 divided doses for 10-84 days. Up to 1,600 milligrams has been taken for up to two weeks for the treatment of cholestasis. For depression, 800-1,600 milligrams daily was the most commonly used dosage range in clinical studies, for up to six weeks. For fibromyalgia, 400 milligrams twice daily has been used. For intrahepatic cholestasis of pregnancy, 500 milligrams given twice daily has been used. For general liver disease, 600-1,200 milligrams daily has also been used.
- As an injection into the muscle, the most common dose for SAME is 200-400 milligrams for 2-4 weeks. Both S-adenosyl-L-methionine 1,4-butanedisulphonate stable salt and disulfate-p-toluenesulfonate stable salt have been studied as injections. 500mg SAME twice daily has also been delivered in a slow running infusion for twelve days followed by oral administration of 500mg twice daily. Injections should only be given under the supervision of a qualified healthcare professional, including a pharmacist.

Children (younger than 18 years):

- There is no proven safe or effective dose for SAME in children.

SAFETY

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

- Avoid in individuals with a known allergy or hypersensitivity to S-adenosyl-L-methionine. Flushing, erythema (reddening of the skin), palpitation, dizziness, and nausea (symptoms of an anaphylactic reaction) have been reported.

Side Effects and Warnings

- SAME has been well tolerated in the majority of clinical trials conducted. The most common adverse effects reported are gastrointestinal in nature with nausea being the most frequently reported. Skin rashes have also been reported. Anxiety and hypomania have been reported mainly in trials that have included patients with bipolar disorder. The use of SAME has not been adequately studied in the pediatric and elderly population, in pregnancy other than the third trimester, or during breastfeeding.
- When given as an injection, diluted SAME has caused superficial phlebitis (inflammation of a vein) and tachycardia (increased heart rate), increased perspiration, transient pain at the injection site, arm soreness, flushing, erythema (reddening of the skin), palpitation, dizziness, nausea, pruritus (itching), urticaria ("hives"), and epigastric pain.
- SAME may lower blood sugar levels. Caution is advised in patients with diabetes or hypoglycemia, and in those taking drugs, herbs, or supplements that affect blood sugar. Serum glucose levels may need to be monitored by a qualified healthcare professional, including a pharmacist, and medication adjustments may be necessary.
- When taken by mouth or by injection, SAME may cause a hot sensation and itchiness of the ear, nausea, vomiting, dry mouth, heartburn, blood in the stool, anorexia, mild diarrhea, stomachaches, slight constipation, increased thirst, increased salivation, urinary frequency, intolerable bowel symptoms, gas, and decreased appetite. Anxiety, insomnia, hypomania, hostility, insomnia, elevated mood, psychoactivation, headache, suicidal ideation, hyperactivity, a reduced need for sleep, and bursts of energy have also been reported.

Pregnancy and Breastfeeding

- SAME crosses the placenta. SAME is not recommended in the first trimester or during breastfeeding due to a lack of available scientific evidence. However, SAME has been used in the third trimester for the treatment of intrahepatic cholestasis with no reported adverse effects in the pregnant women or their newborn babies. A single study of SAME included women in second trimester with no adverse effects noted. Use cautiously in women in their third trimester of pregnancy; SAME should only be used in pregnancy if the benefits clearly outweigh the risks.

INTERACTIONS

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs,

herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

Interactions with Drugs

- SAME may lower blood sugar levels. Caution is advised when using medications that may also lower blood sugar. Patients taking drugs for diabetes by mouth or insulin should be monitored closely by a qualified healthcare professional, including a pharmacist. Medication adjustments may be necessary.
- Use cautiously in patients using tricyclic antidepressant drugs, such as clomipramine. Combination of SAME and tricyclic antidepressant drugs may increase the likelihood of adverse effects.

Interactions with Herbs and Dietary Supplements

- SAME may lower blood sugar levels. Caution is advised when using herbs or supplements that may also lower blood sugar. Blood glucose levels may require monitoring, and doses may need adjustment.

AUTHOR INFORMATION

- This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

REFERENCES

Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com. Selected references are listed below.

1. Arnold O, Saletu B, Anderer P, et al. Double-blind, placebo-controlled pharmacodynamic studies with a nutraceutical and a pharmaceutical dose of ademetionine (SAME) in elderly subjects, utilizing EEG mapping and psychometry. *Eur.Neuropsychopharmacol.* 2005;15(5):533-543. [View Abstract](#)
2. Binder T, Salaj P, Zima T, et al. Randomized prospective comparative study of ursodeoxycholic acid and S-adenosyl-L-methionine in the treatment of intrahepatic cholestasis of pregnancy. *J Perinat Med* 2006;34(5):383-91. [View Abstract](#)
3. Bogarapu S, Bishop JR, Krueger CD, et al. Complementary medicines in pediatric bipolar disorder. *Minerva Pediatr* 2008 Feb;60(1):103-14. [View Abstract](#)
4. Bradley JD, Flusser D, Katz BP, et al. A randomized, double blind, placebo controlled trial of intravenous loading with S-adenosylmethionine (SAM) followed by oral SAM therapy in patients with knee osteoarthritis. *J Rheumatol.* 1994;21(5):905-911. [View Abstract](#)
5. Burrows RF, Clavisi O, Burrows E. Interventions for treating cholestasis in pregnancy (Cochrane Review). *Cochrane Database Syst Rev* 2001;4:CD000493. [View Abstract](#)
6. Mato JM, Camara J, Fernandez de Paz, et al. S-adenosylmethionine in alcoholic liver cirrhosis: a randomized, placebo-controlled, double-blind, multicenter clinical trial. *J Hepatol* 1999;30(6):1081-1089. [View Abstract](#)
7. Mato JM, Lu SC. Role of S-adenosyl-L-methionine in liver health and injury. *Hepatology* 2007 May;45(5):1306-12. [View Abstract](#)
8. Muscettola G, Galzenati M, Balbi A. SAME versus placebo: a double blind comparison in major depressive disorders. *Advances in Biochemical Psychopharmacology* 1982;32:151-156. [View Abstract](#)
9. Nicastrì PL, Diaferia A, Tartagni M, et al. A randomised placebo-controlled trial of ursodeoxycholic acid and S-adenosylmethionine in the treatment of intrahepatic cholestasis of pregnancy. *Br J Obstet.Gynaecol.* 1998;105(11):1205-1207. [View Abstract](#)
10. Ribalta J, Reyes H, Gonzalez MC, et al. S-adenosyl-L-methionine in the treatment of patients with intrahepatic cholestasis of pregnancy: a randomized, double-blind, placebo-controlled study with negative results. *Hepatology* 1991;13(6):1084

1089. [View Abstract](#)

11. Rambaldi A, Gluud C. S-adenosyl-L-methionine for alcoholic liver diseases. Cochrane Database Syst Rev 2006 Apr 19;(2):CD002235. [View Abstract](#)
12. Roncaglia N, Locatelli A, Bellini P, et al. A randomized controlled trial of ursodeoxycholic acid and S-adenosyl-L-methionine in the treatment of gestational cholestasis. Am J Obstet Gynecol 2000;182(1 pt 2):S167.
13. Roncaglia N, Locatelli A, Arreghini A, et al. A randomised controlled trial of ursodeoxycholic acid and S-adenosyl-L-methionine in the treatment of gestational cholestasis. BJOG 2004;111(1):17-21. [View Abstract](#)
14. Tavoni A, Vitali C, Bombardieri S, et al. Evaluation of S-adenosylmethionine in primary fibromyalgia. A double-blind crossover study. Am J Med 11-20-1987;83(5A):107-110. [View Abstract](#)
15. Volkmann H, Norregaard J, Jacobsen S, et al. Double-blind, placebo-controlled cross-over study of intravenous S-adenosyl-L-methionine in patients with fibromyalgia. Scand J Rheumatol. 1997;26(3):206-211. [View Abstract](#)



Natural Standard Monograph (www.naturalstandard.com)

Copyright © 2010 Natural Standard Inc. Commercial distribution or reproduction prohibited.

The information in this monograph is intended for informational purposes only, and is meant to help users better understand health concerns. Information is based on review of scientific research data, historical practice patterns, and clinical experience. This information should not be interpreted as specific medical advice. Users should consult with a qualified healthcare provider for specific questions regarding therapies, diagnosis and/or health conditions, prior to making therapeutic decisions.