Ademetionine *(rINN)*

Ademethionine; Ademetioniini; Adémétionin; Ademetionin; Ademetionina; Ademetioninum; *S*-Adenosyl-L-methionine; Methioninyl adenylate; SAMe. (*S*)-5′-[(3-Amino-3-carboxypropyl)methylsulphonio]-5′-deoxyadenosine hydroxide, inner salt.

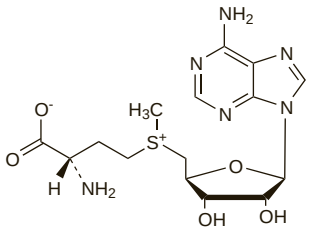
Адеметионин

$C_{15}H_{22}N_6O_5S$ = 398.4.

CAS — 29908-03-0; 485-80-3; 17176-17-9.

ATC — A16AA02.

ATC Vet — QA16AA02.



Profile

Ademetionine is a naturally occurring molecule found in virtually all body tissues and fluids. It acts as a methyl group donor in many transmethylation reactions and therefore is involved in the synthesis or metabolism of a wide range of compounds that maintain normal cell function. Ademetionine sulfate tosilate and ademetionine butanedisulfonate are stable forms of ademetionine that have been used for the treatment of depression (see below), liver disorders, and osteoarthritis.

◊ References.

1. Bottiglieri T, *et al.* The clinical potential of ademetionine (S-adenosylmethionine) in neurological disorders. *Drugs* 1994; **48:** 137–52.
2. Chavez M. SAMe: S-adenosylmethionine. *Am J Health-Syst Pharm* 2000; **57:** 119–23.
3. Fetrow CW, Avila JR. Efficacy of the dietary supplement S-adenosyl-L-methionine. *Ann Pharmacother* 2001; **35:** 1414–25.
4. Bottiglieri T. S-Adenosyl-L-methionine (SAMe): from the bench to the bedside—molecular basis of a pleiotrophic molecule. *Am J Clin Nutr* 2002; **76** (suppl): 1151S–1157S.
5. Gören JL, *et al.* Bioavailability and lack of toxicity of S-adenosyl-L-methionine (SAMe) in humans. *Pharmacotherapy* 2004; **24:** 1501–7.

Depression. Ademetionine has been given orally or parenterally in the management of depression (p.373). It appears to be of similar efficacy to the tricyclic antidepressants but evidence is limited to small, heterogeneous groups of patients studied over short periods of time; additionally many studies have involved parenteral rather than oral therapy.

References.

1. Bressa GM. S-Adenosyl-1-methionine (SAMe) as antidepressant: meta-analysis of clinical studies. *Acta Neurol Scand* 1994; **154** (suppl): 7–14.
2. Anonymous. SAMe for depression. *Med Lett Drugs Ther* 1999; **41:** 107–8.
3. Mischoulon D, Fava M. Role of *S*-adenosyl- -methionine in the treatment of depression: a review of the evidence. *Am J Clin Nutr* 2002; **76:** 1158S–1161S.
4. Papakostas GI, *et al.* S-Adenosyl-methionine in depression: a comprehensive review of the literature. *Curr Psychiatry Rep* 2003; **5:** 460–6.

Liver disorders. Some workers have found that ademetionine produced clinical improvement in patients with **intrahepatic cholestasis**,[1,2] including that associated with pregnancy.[3,4] Pruritus associated with the condition has also been relieved. Other studies,[5,6] however, have not found any benefit.

Ademetionine produced a good or excellent clinical response in patients with **hepatic steatosis**.[7] In a study[8] of patients with **alcoholic liver cirrhosis**, treated with ademetionine for 2 years, there was a trend towards reduced overall mortality or need for liver transplantation, but only in patients with less severe hepatic dysfunction. However, a systematic review[9] of 9 randomised placebo-controlled studies, which included the latter study could not find evidence to support or refute the claim that ademetionine has a beneficial effect in patients with alcoholic liver diseases, and larger high quality randomised placebo-controlled studies are needed.

1. Frezza M, *et al.* Oral S-adenosylmethionine in the symptomatic treatment of intrahepatic cholestasis: a double-blind, placebo-controlled study. *Gastroenterology* 1990; **99:** 211–15.
2. Almasio P, *et al.* Role of S-adenosyl- -methionine in the treatment of intrahepatic cholestasis. *Drugs* 1990; **40** (suppl 3): 111–23.
3. Bonfirraro G, *et al.* S-Adenosyl- -methionine (SAMe)-induced amelioration of intrahepatic cholestasis of pregnancy: results of an open study. *Drug Invest* 1990; **2:** 125–8.
4. Frezza M, *et al.* S-Adenosylmethionine for the treatment of intrahepatic cholestasis of pregnancy: results of a controlled clinical trial. *Hepatogastroenterology* 1990; **37** (suppl 2): 122–5.
5. Ribalta J, *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:** 1084–9.
6. Floreani A, *et al.* S-Adenosylmethionine versus ursodeoxycholic acid in the treatment of intrahepatic cholestasis of pregnancy: preliminary results of a controlled trial. *Eur J Obstet Gynecol Reprod Biol* 1996; **67:** 109–13.
7. Caballeria E, Moreno J. Therapeutic effects of S-adenosylmethionine (SAMe) in hepatic steatosis. *Acta Ther* 1990; **16:** 253–64.
8. Mato JM, *et al.* S-Adenosylmethionine in alcoholic liver cirrhosis: a randomized, placebo-controlled, double-blind, multicenter clinical trial. *J Hepatol* 1999; **30:** 1081–9.
9. Rambaldi A, Gluud C. S-Adenosyl-L-methionine for alcoholic liver diseases. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 01/04/08).

Osteoarthritis. Ademetionine has been reported to possess therapeutic efficacy in the treatment of osteoarthritis (p.11) and similar conditions, possibly due to an effect on cartilage metabolism and formation of anti-inflammatory mediators within the cell; it may also inhibit leukotrienes but does not appear markedly to interfere with prostaglandin synthesis.

References.

1. Domljan Z, *et al.* A double-blind trial of ademethionine vs naproxen in activated gonarthrosis. *Int J Clin Pharmacol Ther Toxicol* 1989; **27:** 329–33.
2. Bradley JD, *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:** 905–11.
3. Soeken KL, *et al.* Safety and efficacy of S-adenosylmethionine (SAMe) for osteoarthritis. *J Fam Pract* 2002; **51:** 425–30.
4. Najm WI, *et al.* S-Adenosyl methionine (SAMe) versus celecoxib for the treatment of osteoarthritis symptoms: a double-blind cross-over trial. *BMC Musculoskelet Disord* 2004; **5:** 6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Transmetil†; Tunik; ***Austral.:*** MoodLift†; ***Cz.:*** Transmetil; ***Ger.:*** Gumbaral; ***Ital.:*** Donamet; Isimet†; Samyr; Transmetil; ***Mex.:*** Samyr; ***Rus.:*** Heptor (Гептор); Heptral (Гептрал); ***Spain:*** S Amet†.

Multi-ingredient: ***Arg.:*** Tunik B12.

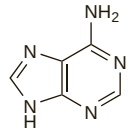
Adenine

Adeniini; Adenin; Adenina; Adeninas; Adénine; Adeninum; Vitamin B_4; Vitamina B_4. 6-Aminopurine; 1,6-Dihydro-6-iminopurine.

Аденин

$C_5H_5N_5$ = 135.1.

CAS — 73-24-5.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Adenine). A white or almost white powder. Very slightly soluble in water and in alcohol; dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides.

USP 31 (Adenine). Odourless white crystals or crystalline powder. Very slightly soluble in water; sparingly soluble in boiling water; slightly soluble in alcohol; practically insoluble in chloroform and in ether.

Profile

Adenine is a purine base and one of the components of adenosine nucleotides that form nucleic acids (p.2355). It is also a constituent of many coenzymes. It has been used to extend the storage life of whole blood (p.1056) and has also been given for the management of white blood cell disorders and alcoholism. Adenine hydrochloride has been used similarly.

Preparations

USP 31: Anticoagulant Citrate Phosphate Dextrose Adenine Solution.

Proprietary Preparations (details are given in Part 3)
Fr.: Leuco-4.

Multi-ingredient: ***Fr.:*** TTD-B -B ; ***Philipp.:*** Godex; ***Rus.:*** Lidevine (Лидевин); ***Spain:*** Hepadif.

Adenosine Phosphate *(BAN, USAN, rINN)*

Adenosine Monophosphate; Adenosine 5′-Monophosphate; Adénosine, Phosphate d'; Adenosine-5′-(dihydrogen phosphate); Adenosine-5′-phosphoric Acid; Adenosini Phosphas; 5′-Adenylic Acid; AMP; A-5MP; Fosfato de adenosina; Monophosadénine; Muscle Adenylic Acid; NSC-20264. 6-Amino-9-β-D-ribofuranosylpurine 5′-(dihydrogen phosphate).

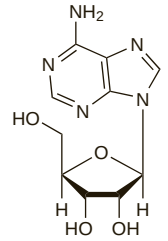
Аденозина Фосфат

$C_{10}H_{14}N_5O_7P$ = 347.2.

CAS — 61-19-8.

ATC — C01EB10.

ATC Vet — QC01EB10.



(adenosine)

Pharmacopoeias. *Ger.* includes the disodium salt ($C_{10}H_{12}N_5Na_2O_7P,xH_2O$).

Profile

Adenosine phosphate is an endogenous adenine nucleotide involved in many biological processes. Adenosine monophosphate (AMP) is a vasodilator and has been included in preparations for venous insufficiency, haemorrhoids, and varicose veins. It has also been used in pain and inflammation. Adenosine diphosphate and its disodium salt have also been used. AMP is also used in bronchial challenge tests to assess airway hyper-responsiveness in asthma and other respiratory disorders.

Unlike adenosine (p.1202) or adenosine triphosphate (below), adenosine phosphate is not used in supraventricular tachycardias.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Adenyl.

Multi-ingredient: ***Cz.:*** Laevadosin†; ***S.Afr.:*** Lipostabil†; ***Spain:*** Artri; Taurobetina†.

Adenosine Triphosphate

Adenosina, trifosfato de; Adenosine 5′-Triphosphate; 5′-Adenyldiphosphoric Acid; Adenylpyrophosphoric Acid; ATP; Trifosadenina; Triphosadénine. Adenosine 5′-(tetrahydrogen triphosphate).

Аденозинтрифосфат

$C_{10}H_{16}N_5O_{13}P_3$ = 507.2.

CAS — 56-65-5.

ATC — C01EB10.

ATC Vet — QC01EB10.

Pharmacopoeias. *Ger.* includes the disodium salt ($C_{10}H_{14}N_5Na_2O_{13}P_3$ = 551.1).

Profile

Adenosine triphosphate (ATP) is an endogenous adenine nucleotide with a fundamental role in cellular energy transformation; ATP is hydrolysed to adenosine diphosphate (ADP) releasing energy stored in phosphate bonds. In addition, extracellular ATP influences many biological processes.

ATP is a vasodilator that has been used in varied disorders. The sodium and disodium salts have been used in cerebral and peripheral vascular disorders and also for the treatment of supraventricular tachycardias, although adenosine (p.1202) is the form generally used as an antiarrhythmic. ATP has also been investigated for use in cachexia in patients with cancer.

◊ Reviews.

1. Agteresch HJ, *et al.* Adenosine triphosphate: established and potential clinical applications. *Drugs* 1999; **58:** 211–32.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Atepadene†; ***Fr.:*** Atepadene; Striadyne; ***Hong Kong:*** ATP-Daiichi; ***Jpn:*** Adetphos; ***Philipp.:*** Nutaphake; ***Rus.:*** Fosfobion (Фосфобион)†; ***Spain:*** Atepodin.

Multi-ingredient: ***Cz.:*** Laevadosin†; ***Indon.:*** Enerplus; Myoviton; Vitap; ***Spain:*** Refulgin.

Adiphenine *(rINN)*

Adifenina; Adiphénine; Adipheninum. 2-Diethylaminoethyl diphenylacetate.

Адифенин

$C_{20}H_{25}NO_2$ = 311.4.

CAS — 64-95-9.