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Acetarsol (BAN, rINN)

Acetaminohydroxyphenylarsonsäure; Acétarsol; Acetarsolum; Acetarsone; Acetphenarsinum; Asetarsoli; Osarsolum. 3-Acetamido-4-hydroxyphenylarsonic acid.

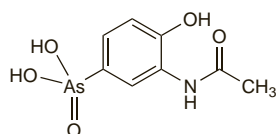
Ацетарсол

$C_8H_{10}AsNO_5$ = 275.1.

CAS — 97-44-9.

ATC — A07AX02; G01AB01; P01CD02.

ATC Vet — QA07AX02; QG01AB01; QP51AD05.



Profile

Acetarsol, a pentavalent organic arsenical derivative, was formerly given orally in the treatment of intestinal amoebiasis and vaginally in the treatment of trichomoniasis, but the use of pentavalent arsenical compounds has been abandoned in favour of more effective and less toxic drugs. For the adverse effects of arsenic and their treatment, see Arsenic Trioxide, p.2260.

Acetarsol suppositories were once tried in the treatment of proctitis. Acetarsol lithium and acetarsol sodium have been included in some preparations for minor mouth infections.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Rus.: Osarbon (Осарбон).

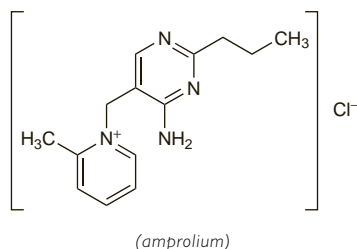
Amprolium Hydrochloride (BANM, rINNM)

Amprolii Hydrochloridum; Amprolium, Chlorhydrate d'; Hidrocloruro de amprolio. 1-(4-Amino-2-propylpyrimidin-5-ylmethyl)-2-methylpyridinium chloride hydrochloride.

Ампролия Гидрохлорид

$C_{14}H_{19}ClN_4$ ·HCl = 315.2.

CAS — 121-25-5 (amprolium); 137-88-2 (amprolium hydrochloride).



Pharmacopoeias. In *Fr.* and *US* for veterinary use only. Also in *BP(Vet)*.

BP(Vet) 2008 (Amprolium Hydrochloride). A white or almost white, odourless or almost odourless powder. Freely soluble in water; slightly soluble in alcohol; practically insoluble in chloroform; very slightly soluble in ether.

USP 31 (Amprolium). A white to light yellow powder. Freely soluble in water, in alcohol, in dimethylformamide and in methyl alcohol; sparingly soluble in dehydrated alcohol; practically insoluble in acetone, in butyl alcohol, and in isopropyl alcohol.

Profile

Amprolium hydrochloride is an antiprotozoal used in veterinary practice, alone or with other drugs such as ethopabate, for the control of coccidiosis in pigeons and in poultry.

Pentavalent Antimony Compounds

Antimonio pentavalente, compuestos de.

Meglumine Antimonate

Antimoniato de meglumina; Antimony Meglumine; Meglumine Antimoniate; Protostib; RP-2168. 1-Deoxy-1-methylamino-D-glucitol antimonate.

Меглумина Антимонат

$C_7H_{18}NO_8Sb$ = 366.0.

CAS — 133-51-7.

ATC — P01CB01.

ATC Vet — QP51AB01.

Sodium Stibogluconate (BAN, rINN)

Estibogluconato de sodio; Natrii Stibogluconas; Natriumstibogluconaat; Natriumstibogluconat; Sod. Stiboglucon; Sodium Antimony Gluconate; Sodyum Stibogluconat; Stibogluconate de Sodium; Stibogluconat-Natrium.

Натрия Стибоглюконат

CAS — 16037-91-5.

ATC — P01CB02.

ATC Vet — QP51AB02.

Description. A pentavalent antimony compound of indefinite composition. It has been represented by the formula $C_6H_9Na_2O_9Sb$ but usually there are less than 2 atoms of Na for each atom of Sb. Solutions may be sterilised by autoclaving.

Pharmacopoeias. In *Br.*, *Chin.*, *Int.*, and *It.*

BP 2008 (Sodium Stibogluconate). It is mainly the disodium salt of μ -oxy-bis[gluconato(3- O^2 , O^3 , O^4 -hydroxy-antimony)]. It contains not less than 30.0% and not more than 34.0% of antimony(V), calculated with reference to the dried and methanol-free substance. It is a colourless, odourless or almost odourless, mostly amorphous powder. Very soluble in water; practically insoluble in alcohol and in ether. A solution in water containing 10% of pentavalent antimony has a pH of 5.0 to 5.6 after autoclaving.

Adverse Effects, Treatment, and Precautions

As for Trivalent Antimony Compounds, p.141.

Adverse effects are generally less frequent and less severe with the pentavalent antimony compounds sodium stibogluconate and meglumine antimonate than with trivalent compounds such as antimony sodium tartrate. Nevertheless, similar precautions should be observed, especially in patients on high-dose therapy. Intramuscular injections of sodium stibogluconate can be painful and intravenous use has been associated with thrombophlebitis.

Common adverse effects of pentavalent antimony are anorexia, vomiting, nausea, malaise, arthralgia and myalgia, headache, lethargy, and pancreatitis. ECG changes are dose-dependent and most commonly include T-wave inversion and prolonged QT interval. Renal damage is a rarely reported toxic effect. Pentavalent antimony is usually well tolerated. Serious adverse effects when they occur usually involve the liver or the heart when it is prudent to interrupt the course temporarily.

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- WHO. Control of the leishmaniasis. *WHO Tech Rep Ser* 793 1990. Available at: http://libdoc.who.int/trs/WHO_TRS_793.pdf (accessed 17/07/08)
- Aronson NE, *et al.* Safety and efficacy of intravenous sodium stibogluconate in the treatment of leishmaniasis: recent US military experience. *Clin Infect Dis* 1998; **27**: 1457–64.

Breast feeding. The amount of antimony distributed into the breast milk of a patient given sodium stibogluconate was considered not to constitute a hazard and oral absorption was not detected in an animal study.¹ The American Academy of Pediatrics also considers that the use of antimony is usually compatible with breast feeding.² Others, however, have felt that more safety evaluation was required before antimony could be considered completely safe during breast feeding.³

- Berman JD, *et al.* Concentration of Pentostam in human breast milk. *Trans R Soc Trop Med Hyg* 1989; **83**: 784–5.
- American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108**: 776–89. Correction. *ibid.*: 1029. Also available at: <http://aapolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776> (accessed 02/06/04)
- Verschoyle RD. Comment. *Trop Dis Bull* 1990; **87**: 919.

Effects on the blood. Although thrombocytopenia is associated with leishmaniasis, there are case reports of it also being associated with sodium stibogluconate.^{1,2}

- Braconier JH, Miörner H. Recurrent episodes of thrombocytopenia during treatment with sodium stibogluconate. *J Antimicrob Chemother* 1993; **31**: 187–8.
- Hepburn NC. Thrombocytopenia complicating sodium stibogluconate therapy for cutaneous leishmaniasis. *Trans R Soc Trop Med Hyg* 1993; **87**: 691.

Effects on the heart. The ECG was monitored during 65 courses of treatment with sodium stibogluconate in 59 Kenyan

patients with leishmaniasis.¹ ECG abnormalities developed during 35 treatment courses. They were qualitatively similar to those previously described during treatment with trivalent antimonial drugs, but occurred less frequently and later during the course of treatment. The most common abnormality was inversion and/or decreased amplitude of T waves. Incidence was related to total daily dose and duration of treatment. One patient died suddenly during the 4th week of treatment with antimony 60 mg/kg daily. Other deaths probably related to cardiac toxicity have been reported in patients receiving 60 mg/kg daily² and 30 mg/kg daily.³ It has been recommended¹ that for treatment with sodium stibogluconate ECGs should be obtained every 3 to 4 days in patients given antimony 20 mg/kg daily for more than 20 days or a higher dose for more than 10 days. If Stokes-Adams attacks or ventricular tachyarrhythmias develop, sodium stibogluconate should be stopped and appropriate treatment given. A retrospective study⁴ in patients treated with sodium stibogluconate for mostly cutaneous leishmaniasis found that the mean QTc interval steadily increased throughout the period of treatment, reaching a potentially toxic threshold by the third week, but cardiotoxicity was seen only in one elderly patient who had hypokalaemia and pre-existing cardiovascular morbidity. Identification before treatment of factors that may increase cardiovascular risk is important.

- Chulay JD, *et al.* Electrocardiographic changes during treatment of leishmaniasis with pentavalent antimony (sodium stibogluconate). *Am J Trop Med Hyg* 1985; **34**: 702–9.
- Bryceson ADM, *et al.* Visceral leishmaniasis unresponsive to antimonial drugs II: response to high dosage sodium stibogluconate or prolonged treatment with pentamidine. *Trans R Soc Trop Med Hyg* 1985; **79**: 705–14.
- Thakur CP. Harmful effect of high stibogluconate treatment of kala-azar in India. *Trans R Soc Trop Med Hyg* 1986; **80**: 672–3.
- Lawn SD, *et al.* Electrocardiographic and biochemical adverse effects of sodium stibogluconate during treatment of cutaneous and mucosal leishmaniasis among returned travellers. *Trans R Soc Trop Med Hyg* 2006; **100**: 264–9.

Effects on the kidneys. Sodium stibogluconate given for 10 days to 16 young men with cutaneous leishmaniasis had no apparent adverse effect on glomerular or tubular renal function.¹ However, evidence of renal tubular dysfunction has been reported in patients with mucocutaneous leishmaniasis given meglumine antimonate or sodium stibogluconate for 30 days or more² and acute renal failure has occurred in patients both with³ and without⁴ pre-existing renal impairment, the latter resulting in death.

- Joliffe DS. Nephrotoxicity of pentavalent antimonials. *Lancet* 1985; **i**: 584.
- Veiga JPR, *et al.* Renal tubular dysfunction in patients with mucocutaneous leishmaniasis treated with pentavalent antimonials. *Lancet* 1983; **ii**: 569.
- Balzan M, Fenech F. Acute renal failure in visceral leishmaniasis treated with sodium stibogluconate. *Trans R Soc Trop Med Hyg* 1992; **86**: 515–16.
- Rodrigues MLO, *et al.* Nephrotoxicity attributed to meglumine antimonate (Glucantime) in the treatment of generalized cutaneous leishmaniasis. *Rev Inst Med Trop Sao Paulo* 1999; **41**: 33–7.

Effects on the liver. WHO has reported that when serious adverse effects occur with sodium stibogluconate they usually involve the liver or the heart.¹ There have been reports of disturbed liver function^{2,3} in patients given sodium stibogluconate, although there has also been a report⁴ that signs of altered liver function, which may be a feature of visceral leishmaniasis, improved during treatment with sodium stibogluconate.

- WHO. Control of the leishmaniasis. *WHO Tech Rep Ser* 793 1990. Available at: http://libdoc.who.int/trs/WHO_TRS_793.pdf (accessed 17/07/08)
- Ballou WR, *et al.* Safety and efficacy of high-dose sodium stibogluconate therapy of American cutaneous leishmaniasis. *Lancet* 1987; **ii**: 13–16.
- Hepburn NC, *et al.* Hepatotoxicity of sodium stibogluconate in leishmaniasis. *Lancet* 1993; **342**: 238–9.
- Misbahuddin M, *et al.* Stibogluconate for leishmaniasis. *Lancet* 1993; **342**: 804.

Effects on the musculoskeletal system. Arthralgia is common with pentavalent antimony compounds. It is usually dose-dependent¹ but a patient has been described who experienced symptoms early in treatment.² Palindromic arthropathy with effusion was associated with sodium stibogluconate treatment in another patient.³

- Ballou WR, *et al.* Safety and efficacy of high-dose sodium stibogluconate therapy of American cutaneous leishmaniasis. *Lancet* 1987; **ii**: 13–16.
- Castro C, *et al.* Severe arthralgia, not related to dose, associated with pentavalent antimonial therapy for mucosal leishmaniasis. *Trans R Soc Trop Med Hyg* 1990; **84**: 362.
- Donovan KL, *et al.* Pancreatitis and palindromic arthropathy with effusions associated with sodium stibogluconate treatment in a renal transplant recipient. *J Infect* 1990; **21**: 107–10.

Effects on the nervous system. Peripheral neuropathy developed in a patient about 8 days after starting therapy with sodium stibogluconate.¹ The symptoms were generally reversible when treatment was stopped (after 17 days), although there was some slight persistent hypoesthesia in the toes. An interaction with a single dose of amitriptyline, taken on the second day of stibogluconate therapy, seemed unlikely but could not be ruled out.

- Brummitt CF, *et al.* Reversible peripheral neuropathy associated with sodium stibogluconate therapy for American cutaneous leishmaniasis. *Clin Infect Dis* 1996; **22**: 878–9.