2. Chrubasik S, *et al.* Treatment of low back pain with a herbal or synthetic anti-rheumatic: a randomized controlled study. Willow bark extract for low back pain. *Rheumatology (Oxford)* 2001; **40:** 1388–93.
3. Gagnier JJ, *et al.* Herbal medicine for low back pain. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 05/10/06).
4. Biegert C, *et al.* Efficacy and safety of willow bark extract in the treatment of osteoarthritis and rheumatoid arthritis: results of 2 randomized double-blind controlled trials. *J Rheumatol* 2004; **31:** 2121–30.

Preparations

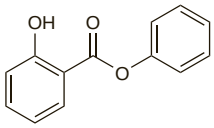
Proprietary Preparations (details are given in Part 3)
Braz.: Zortrix; ***Ger.:*** Assalix; Assplant; Lintia†; Rheumakaps; Rheumatab Salicis†; ***Pol.:*** Salicortex; ***Switz.:*** Assalix.

Multi-ingredient: ***Austral.:*** Arthritic Pain Herbal Formula 1; Bioglan Arthri Plus; Extralife Migrai-Care; Extralife PMS-Care; Guaiacum Complex†; Lifesystem Herbal Formula 1 Arthritic Aid†; Prost-1†; ***Austria:*** Digestodoron; ***Braz.:*** Calman; Calmiplan; Floriny; Pasalix; Pasic; Passi Catha†; Passiflorine; ***Cz.:*** Antirevmaticky Caj; Erkaltungstee†; Valofyt Neo; ***Fr.:*** Arkophytum†; Mediflor Tisane Circulation du Sang No 12; Phytheol; ***Ger.:*** Digestodoron; Dr Wiemanns Rheumatonikum; ***Ital.:*** Biothymus DS; Bodyguard; Donalg; Influ-Zinc; Nepiros; Nevril; Passiflorine; Reumafort; ***Malaysia:*** Celery Plus†; ***Mex.:*** Ifupasil; ***Pol.:*** Enterosol; Pyrosal; Reumacor; Reumosol; Termasil; ***Port.:*** Neurocardol†; ***S.Afr.:*** Digestodoron; ***Spain:*** Dolosul†; Jaquesor†; Mesatil†; Natusor Harpagosinol†; Natusor Jaquesan†; ***Switz.:*** Dragees antirhumatismales; Strath Gouttes Rhumatisme; Tisane antirhumatismale; ***UK:*** Bio-Strath Willow Formula; Gerard House Reumalex; Herbal Pain Relief; St Johnswort Compound; ***Venez.:*** Passiflorum.

Salol

Benzofenolsalicylaat; Benzophénol Salicylate; Fenylsalicylat; Fenylu salicylan; Fenyylisalisylaatti; Phenyli Salicylas; Phenylis Salicylas; Salicilato de fenilo. Phenyl salicylate.

$C_{13}H_{10}O_3$ = 214.2.
CAS — 118-55-8.
ATC — G04BX12.
ATC Vet — QG04BX12.



Pharmacopoeias. In *Pol.*

Profile

Salol is a salicylic acid derivative (see Aspirin, p.20). It was formerly used as an intestinal antiseptic, but effective doses were toxic owing to the liberation of phenol. It is used in oral preparations containing methenamine for the treatment of lower urinary-tract infections.

Salol has been used topically as a sunscreen.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Aussie Tan Sunstick.

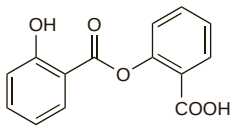
Multi-ingredient: ***Arg.:*** Dermithan; ***Austria:*** Carl Baders Divinal; ***Belg.:*** Borostyrol; ***Braz.:*** Talco Alivio†; ***Canad.:*** Franzbranns†; ***Chile:*** Galutec†; Polisep†; ***Cz.:*** Parodontal F5†; ***Fr.:*** Borostyrol; Dermophil Indien†; Nisacalm; ***Pol.:*** Salotannal; Urosal; ***Switz.:*** Borostyrol N†; Dermophil Indien; GU Eau†; Penta; ***Turk.:*** Sandolin; ***USA:*** Atrosept; Dolsed†; MHP-A; MSP-Blu; Prosed/DS; Trac Tabs 2X†; UAA; Urelle; Uretron; Uridon Modified†; Urimar-T; Urimax; Urised; Uriseptic; UriSym†; Uritact; Uro Blue; Urogesic Blue; Utira.

Salsalate *(BAN, USAN, rINN)*

NSC-49171; Salicyl Salicylate; Salicylosalicylic Acid; Salicylsalicylic Acid; Salsalato; Salsalatum; Salysal; Sasapyrine. *O*-(2-Hydroxybenzoyl)salicylic acid.

Сальсалат

$C_{14}H_{10}O_5$ = 258.2.
CAS — 552-94-3.
ATC — N02BA06.
ATC Vet — QN02BA06.



Pharmacopoeias. In *Chin.* and *US.*
USP 31 (Salsalate). Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Aspirin, p.20.

The use of aspirin and other acetylated salicylates is generally not recommended for children because of the risk of Reye's syndrome, unless specifically indicated. Some licensed product information extends this precaution to salsalate.

Effects on the gastrointestinal tract. Salsalate is associated with less faecal blood loss than aspirin and has been reported to cause fewer gastric lesions than piroxicam.[1] However, small-bowel ulcerations were reported in a patient when salsalate was added to a regimen of ranitidine and metoclopramide which had been prescribed for duodenal ulcer.[2]

1. Porro GB, *et al.* Salsalate in the treatment of rheumatoid arthritis: a double-blind clinical and gastroscopic trial versus piroxicam: II—endoscopic evaluation. *J Int Med Res* 1989; **17:** 320–3.
2. Souza Lima MA. Ulcers of the small bowel associated with stomach-bypassing salicylates. *Arch Intern Med* 1985; **145:** 1139.

Effects on the kidneys. A case of minimal-change nephrotic syndrome associated with salsalate use.[1]

1. Vallès M, Tovar JL. Salsalate and minimal-change nephrotic syndrome. *Ann Intern Med* 1987; **107:** 116.

Effects on the mouth. Ulcerated lesions on the tongue of a 77-year-old man were caused by taking salsalate tablets incorrectly.[1] The patient had placed the tablets under his tongue rather than swallowing them whole, resulting in prolonged, direct contact with the tongue.

1. Ruscin JM, Astroth JD. Lingual lesions secondary to prolonged contact with salsalate tablets. *Ann Pharmacother* 1998; **32:** 1248.

Interactions

For interactions associated with salicylates, see Aspirin, p.23.

Pharmacokinetics

Salsalate is insoluble in acidic gastric fluids but is soluble in the small intestine. One molecule of salsalate is hydrolysed to 2 molecules of salicylic acid; hydrolysis occurs both in the small intestine and after absorption of the parent compound. Additional details on the pharmacokinetics of salicylic acid are provided in aspirin (see p.23). Not all of the absorbed salsalate is hydrolysed and about 13% of salsalate is excreted as glucuronide conjugates in the urine; thus, the amount of salicylic acid available from salsalate is less than that from aspirin when the two drugs are given in equimolar equivalents of salicylic acid.

Uses and Administration

Salsalate is a salicylic acid derivative that has analgesic, anti-inflammatory, and antipyretic actions similar to those of aspirin (see p.23). It is used for pain and fever and also in inflammatory disorders such as osteoarthritis and rheumatoid arthritis. A usual oral dose is up to 3 g daily given in divided doses with food.

Preparations

USP 31: Salsalate Capsules; Salsalate Tablets.

Proprietary Preparations (details are given in Part 3)
USA: Amigesic; Argesic-SA; Artha-G; Disalcid; Marthritic; Mono-Gesic†; Salflex; Salsitab.

Sarracenia Purpurea

Pitcher Plant.

Profile

The roots and leaves of *Sarracenia purpurea* (Sarraceniaceae) have been used in the form of an aqueous distillate, given by local injection, for neuromuscular or neuralgic pain.

Preparations

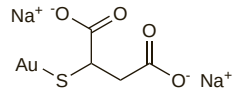
Proprietary Preparations (details are given in Part 3)
USA: Sarapin.

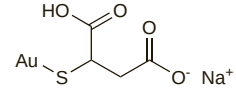
Sodium Aurothiomalate *(rINN)*

Aurothiomalate de Sodium; Aurotiomalato de sodio; Gold Sodium Thiomalate; Natrii aurothiomalas; Natrium-aurothiomalát; Natriumaurotiomalaatti; Natriumaurotiomalat; Sodium, aurothiomalate de; Sodium Aurothiosuccinate; Sodu aurotiojabłczan; Sodyum Orotiyomalat.

Натрия Ауротиомалат

CAS — 12244-57-4 (anhydrous xNa); 39377-38-3 (disodium monohydrate).
ATC — M01CB01.
ATC Vet — QM01CB01.





Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Sodium Aurothiomalate). A mixture of monosodium and disodium salts of (2*RS*)-2-(aurosulphanyl)butanedioic acid. It contains 44.5 to 46.0% of gold and 10.8 to 11.8% of sodium, calculated with reference to the dried substance. A fine, pale yellow, hygroscopic powder. Very soluble in water; practically insoluble in alcohol and in dichloromethane. A 10% solution in water has a pH of 6.0 to 7.0. Store in airtight containers.
USP 31 (Gold Sodium Thiomalate). A mixture of the monosodium and disodium salts of gold thiomalic acid [(aurothio)succinic acid] ($C_4H_4AuNaO_4S$ = 368.1 and $C_4H_3AuNa_2O_4S$ = 390.1) that has a gold content of 44.8 to 49.6%, and 49.0 to 52.5% calculated on the dried alcohol-free and glycerol-free material. pH of a 10% solution in water is between 5.8 and 6.5. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Adverse Effects

Reports show a wide range for the incidence of adverse effects of sodium aurothiomalate. However, some consider that with careful treatment about one-third of patients will experience adverse effects. It is also considered that about 5% of patients will experience severe adverse effects and that some of the effects will be fatal. The most common effects involve the skin and mucous membranes with pruritus (an early sign of intolerance) and stomatitis (often with a metallic taste) being the most prominent. Rashes with pruritus often occur after 2 to 6 months of intramuscular treatment and may require stopping therapy. Other reactions affecting the skin and mucous membranes include erythema, maculopapular eruptions, erythema multiforme, urticaria, eczema, seborrhoeic dermatitis, lichenoid eruptions, alopecia, exfoliative dermatitis, glossitis, pharyngitis, vaginitis, photosensitivity reactions, and irreversible pigmentation (chrysiasis).

Toxic effects on the blood include eosinophilia, thrombocytopenia, leucopenia, agranulocytosis, and aplastic anaemia.

Effects on the kidneys include mild transient proteinuria which may lead to heavy proteinuria, haematuria, and nephrosis.

Other effects reported include pulmonary fibrosis, dyspnoea, toxic hepatitis, cholestatic jaundice, peripheral neuritis, encephalitis, psychoses, fever, and gastrointestinal disorders including enterocolitis. Gold deposits may occur in the eyes. Vasomotor or nitritoid reactions, with weakness, flushing, palpitations, and syncope, may occur after injection of sodium aurothiomalate. Local irritation may also follow injection.

Sometimes there is an initial exacerbation of the arthritic condition.

Some adverse effects of gold have an immunogenic component.

◊ Reviews.

1. Tozman ECS, Gottlieb NL. Adverse reactions with oral and parenteral gold preparations. *Med Toxicol* 1987; **2:** 177–89.
2. van Roon EN, *et al.* Parenteral gold preparations. Efficacy and safety of therapy after switching from aurothioglucose to aurothiomalate. *J Rheumatol* 2005; **32:** 1026–30.

Effects on the blood. Blood disorders such as eosinophilia, leucopenia, granulocytopenia, and thrombocytopenia have occurred in patients receiving gold therapy. Eosinophilia has been reported to be the most frequent haematological abnormality.[1] It has been estimated that thrombocytopenia develops in 1 to 3% of patients receiving gold salts.[2]

Fatal consumption coagulopathy occurred in 4 children after the second injection of sodium aurothioglucose or sodium aurothiomalate.[3]

1. Foster RT. Eosinophilia—a marker of gold toxicity. *Can J Hosp Pharm* 1985; **85:** 150–1.
2. Coblyn JS, *et al.* Gold-induced thrombocytopenia: a clinical and immunogenetic study of twenty-three patients. *Ann Intern Med* 1981; **95:** 178–81.
3. Jacobs JC, *et al.* Consumption coagulopathy after gold therapy for JRA. *J Pediatr* 1984; **105:** 674–5.

Effects on the cardiovascular system. Vasomotor or nitritoid reactions associated with gold compounds are usually transient and self-limiting and although they may be mild there have been isolated reports of associated complications such as myocardial infarction, stroke, transient ischaemic attack, and transient monocular visual loss.[1] Most reactions have been associated with sodium aurothiomalate (a reported incidence of 4.7%) but they have also occurred with auranofin and sodium aurothioglucose. Tachyphylaxis usually occurs to the reactions and most patients are able to continue treatment but paradoxically in some the severity increases with repeated doses; 2.8% of patients receiving sodium aurothiomalate may require a change of treatment due to recurrent reactions. It is important to distinguish such reactions from true anaphylactic reactions to gold.[1] Patients taking ACE inhibitors may be at increased risk of nitritoid reactions.[2,3] Transfer of the patient to sodium aurothioglucose or re-

duction of the dose by 50%, injection in the recumbent position, and observation for 20 minutes have been recommended for the next few injections after a reaction.[2]

1. Ho M, Pullar T. Vasomotor reactions with gold. *Br J Rheumatol* 1997; **36:** 154–6.
2. Arthur AB, *et al.* Nitritoid reactions: case reports, review, and recommendations for management. *J Rheumatol* 2001; **28:** 2209–12.
3. Nixon J, Pande I. Gold, nitritoid reactions and angiotensin-converting enzyme inhibitors. *Rheumatology (Oxford)* 2006; **45:** 118–19.

Effects on the gastrointestinal tract. A case report of enterocolitis due to sodium aurothiomalate has been published[1] and 27 other cases associated with gold therapy reviewed. For colitis associated with oral gold see also under Auranofin, p.25.

1. Jackson CW, *et al.* Gold induced enterocolitis. *Gut* 1986; **27:** 452–56.

Effects on the immune system. Details of a patient who developed an immune deficiency syndrome that was attributed to gold therapy with sodium aurothiomalate.[1]

1. Haskard DO, Macfarlane D. Adult acquired combined immune deficiency in a patient with rheumatoid arthritis on gold. *J R Soc Med* 1988; **81:** 548–9.

Effects on the kidneys. Proteinuria developed in 21 patients while receiving a standard regimen of sodium aurothiomalate.[1] The severity of the proteinuria varied greatly and in 11 it increased for 4 months after treatment was stopped. Eight patients were considered to have developed the nephrotic syndrome. The median duration of proteinuria was 11 months, resolving in all 21 patients when treatment was withdrawn; at 24 months 3 patients were still experiencing proteinuria and it was not until 39 months that all were free of the condition. Renal biopsy indicated several types of kidney damage.

See under Auranofin (p.25) for a comparative incidence of proteinuria in patients receiving sodium aurothiomalate or auranofin.

1. Hall CL, *et al.* The natural course of gold nephropathy: long term study of 21 patients. *BMJ* 1987; **295:** 745–8.

Effects on the lungs. 'Gold lung' is the term used to describe symptoms of dyspnoea on exertion, weakness, dry cough, and malaise that are seen rarely in patients on gold treatment.[1] Such symptoms usually develop some weeks or months after starting gold treatment and are associated with cumulative doses of several hundred milligrams although, very rarely, they have been seen with cumulative doses of less than 100 mg.[2] Pulmonary insufficiency may eventually develop and there have been occasional fatalities.[3] The pulmonary lesions usually subside on withdrawal of gold therapy, although persistent symptoms have been reported.

Nonbacterial thrombotic endocarditis associated with gold-induced pulmonary disease has also been reported.[4] This was considered to be a manifestation of gold-induced immune complex deposition.

1. Sinha A, *et al.* Gold-induced pneumonitis: computed tomography findings in a patient with rheumatoid arthritis. *Rheumatology (Oxford)* 2001; **40:** 712–14.
2. Hafejee A, Burke MJ. Acute pneumonitis starting 2 hours after intramuscular gold administration in a patient with rheumatoid arthritis. *Ann Rheum Dis* 2004; **63:** 1525–6.
3. Soler MJ, *et al.* Fatal, gold-induced pneumonitis. *Rheumatol Int* 2003; **23:** 207–10.
4. Kollef MH, *et al.* Nonbacterial thrombotic endocarditis associated with gold induced pulmonary disease. *Ann Intern Med* 1988; **108:** 903–4.

Effects on the nails. A 34-year-old woman with severe rheumatoid arthritis receiving intramuscular gold developed yellow thickened toenails and fingernails after 2 years of treatment.[1] Although there was some improvement in nail growth on stopping treatment, some light yellow discoloration in all 20 nails persisted.

1. Roest MAB, Ratnavel R. Yellow nails associated with gold therapy for rheumatoid arthritis. *Br J Dermatol* 2001; **145:** 855–6.

Effects on the nervous system. Neurological complications with gold salts are infrequent but may include peripheral neuropathy, Guillain-Barré syndrome, myokymia (repeated involuntary contractions of muscle fibre), and encephalopathy. Some reports[1-6] are given below.

1. Dick DJ, Raman D. The Guillain-Barre syndrome following gold therapy. *Scand J Rheumatol* 1982; **11:** 119–20.
2. Schlumpf U, *et al.* Neurologic complications induced by gold treatment. *Arthritis Rheum* 1983; **26:** 825–31.
3. Cerinic MM, *et al.* Gold polyneuropathy in juvenile rheumatoid arthritis. *BMJ* 1985; **290:** 1042.
4. Cohen M, *et al.* Acute disseminated encephalomyelitis as a complication of treatment with gold. *BMJ* 1985; **290:** 1179–80.
5. Dubowitz MN, *et al.* Gold-induced neuroencephalopathy responding to dimercaprol. *Lancet* 1991; **337:** 850–1.
6. Garrido JA, *et al.* Mioquimias inducidas por sales de oro. *Neurologia* 1995; **10:** 235–7.

Effects on the skin. Chrysiasis is a distinctive pigmentation that develops in light-exposed skin of patients receiving parenteral gold salts. In a study[1] of 31 patients with chrysiasis who were receiving intramuscular sodium aurothiomalate for rheumatoid arthritis, it was noted that visible changes developed above a threshold equivalent to 20 mg/kg gold content. The severity of the pigmentation depended upon cumulative dose. Focal aggregates of gold are deposited in the reticular and papillary dermis with no obvious increase in melanin. The pigmentation is permanent but benign, although the cosmetic effects may cause some patients distress. Prevention of chrysiasis is difficult but avoidance of exposure to sunlight may be helpful.

1. Smith RW, *et al.* Chrysiasis revisited: a clinical and pathological study. *Br J Dermatol* 1995; **133:** 671–8.

Hypersensitivity. Many adverse effects associated with gold treatment have an immunological basis. Patients with contact allergy to gold may exhibit a flare-up, associated with cytokine release, when given sodium aurothiomalate intramuscularly.[1] Small amounts of nickel have been detected in sodium aurothiomalate injection[2] and in sodium aurothioglucose injection[3] and it has been suggested that gold therapy may also exacerbate or induce hypersensitivity to nickel.[2-4]

Anaphylaxis may occur occasionally[5] but vasomotor or 'nitritoid' reactions (see Effects on the Cardiovascular System, above) may produce similar symptoms.

1. Möller H, *et al.* The flare-up reactions after systemic provocation in contact allergy to nickel and gold. *Contact Dermatitis* 1999; **40:** 200–4.
2. Choy EHS, *et al.* Nickel contamination of gold salts: link with gold-induced skin rash. *Br J Rheumatol* 1997; **36:** 1054–8.
3. Wijnands MJH, *et al.* Chrysotherapy provoking exacerbation of contact hypersensitivity to nickel. *Lancet* 1990; **335:** 867–8.
4. Fulton RA, *et al.* Another hazard of gold therapy? *Ann Rheum Dis* 1982; **41:** 100–1.
5. Neustadt DH. Another anaphylactic reaction after gold (aurothiomalate) injection. *J Rheumatol* 1995; **22:** 190.

Pancreatitis. It was suggested that pancreatitis reported in a woman receiving gold injections and in a woman on oral gold therapy may have been due to a hypersensitivity reaction.[1]

1. Eisemann AD, *et al.* Pancreatitis and gold treatment of rheumatoid arthritis. *Ann Intern Med* 1989; **111:** 860–1.

Treatment of Adverse Effects

The treatment of the adverse effects of gold is usually symptomatic and most effects resolve when gold therapy is withdrawn. In severe cases a chelator such as dimercaprol (p.1444) may be used.

Precautions

Gold therapy is contra-indicated in exfoliative dermatitis, SLE, necrotising enterocolitis, and pulmonary fibrosis. It should be used with caution in the elderly and in renal or hepatic impairment; use is contra-indicated if renal or hepatic disorders are severe. Patients with a history of haematological disorders or who have previously shown toxicity to heavy metals should not be given gold salts, nor should any severely debilitated patient.

It is recommended that diabetes mellitus and heart failure should be adequately controlled in any patient before gold is given. Patients with a history of urticaria, eczema, or colitis should be treated with caution. Patients with a poor sulfoxidation status may be more susceptible to adverse effects of sodium aurothiomalate.

Use of gold compounds with other therapy capable of inducing blood disorders should be undertaken with caution, if at all.

Because of the risk of vasomotor reactions, patients should remain recumbent for about 10 minutes after each injection.

Urine should be tested for albumin before each injection and a full blood count carried out. Patients receiving gold compounds either orally or parenterally should be warned to report the appearance of sore throat or tongue, metallic taste, pruritus, rash, buccal ulceration, easy bruising, purpura, epistaxis, bleeding gums, unexplained bleeding, menorrhagia, pyrexia, indigestion, diarrhoea, or unexplained malaise. The development of breathlessness or cough should also be reported. Effects such as eosinophilia, proteinuria, pruritus, and rash arising during gold treatment should be allowed to resolve before therapy is continued.

Licensed product information recommends that annual chest X-rays should be carried out.

Breast feeding. The American Academy of Pediatrics considers that gold compounds are usually compatible with breast feeding.[1]

Gold has been detected in breast milk[2-4] and found bound to the red blood cells of breast-fed babies.[3,4] In a report[2] of a breast-fed infant it was calculated that the weight-adjusted dose of gold received by the infant exceeded that received by the mother although the infant exhibited no ill-effects during 100 days of breast feeding and developed normally thereafter. Nonetheless, because of the relatively high exposure it was recommended that breast-fed infants should be closely monitored.

1. 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://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 13/11/06)
2. Bennett PN, *et al.* Use of sodium aurothiomalate during lactation. *Br J Clin Pharmacol* 1990; **29:** 777–9.
3. Needs CJ, Brooks PM. Antirheumatic medication during lactation. *Br J Rheumatol* 1985; **24:** 291–7.
4. Blau SP. Metabolism of gold during lactation. *Arthritis Rheum* 1973; **16:** 777–8.

Porphyria. Sodium aurothiomalate has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Pregnancy. Although healthy neonates have been born after *in-utero* exposure to gold compounds,[1,2] *animal* studies and a report[1] of malformation in a child born to a woman treated with sodium aurothiomalate led to a suggestion that gold might possibly have teratogenic effects. Licensed product information advises that sodium aurothiomalate should be avoided during pregnancy.

1. Rogers JG, *et al.* Possible teratogenic effects of gold. *Aust Paediatr J* 1980; **16:** 194–5.
2. Bennett PN, *et al.* Use of sodium aurothiomalate during lactation. *Br J Clin Pharmacol* 1990; **29:** 777–9.

Interactions

There is an increased risk of toxicity when gold compounds are given with other nephrotoxic, hepatotoxic, or myelosuppressive drugs. Use of gold compounds with penicillamine may increase the risk of haematologic or renal adverse reactions.

ACE inhibitors. For a possible increased risk of nitritoid reactions when gold compounds are given to patients taking ACE inhibitors, see Effects on the Cardiovascular System, above.

Penicillamine. For a discussion on the effects of previous therapy with gold salts affecting penicillamine toxicity, see p.1458.

Pharmacokinetics

Sodium aurothiomalate is absorbed readily after intramuscular injection and 85 to 95% becomes bound to plasma proteins. With doses of 50 mg weekly a steady-state serum concentration of gold of about 3 to 5 micrograms/mL is reached in 5 to 8 weeks. It is widely distributed to body tissues and fluids, including synovial fluid, and accumulates in the body.

The serum half-life of gold is about 5 to 6 days but this increases after successive doses and after a course of treatment, gold may be found in the urine for up to 1 year or more owing to its presence in deep body compartments. Sodium aurothiomalate is mainly excreted in the urine, with smaller amounts in the faeces.

Gold has been detected in the fetus when sodium aurothiomalate was given to the mother. Gold is distributed into breast milk.

◊ Reviews.

1. Blocka KLN, *et al.* Clinical pharmacokinetics of oral and injectable gold compounds. *Clin Pharmacokinet* 1986; **11:** 133–43.
2. Tett SE. Clinical pharmacokinetics of slow-acting antirheumatic drugs. *Clin Pharmacokinet* 1993; **25:** 392–407.

Uses and Administration

Sodium aurothiomalate and other gold compounds are used mainly for their anti-inflammatory effect in active progressive rheumatoid arthritis and progressive juvenile idiopathic arthritis; they may also be beneficial in psoriatic arthritis. They are generally used as disease-modifying antirheumatic drugs in patients whose symptoms are unresponsive to or inadequately controlled by NSAIDs alone.

Sodium aurothiomalate therapy should only be undertaken where facilities are available to carry out the tests specified under Precautions, above.

Sodium aurothiomalate is given by deep intramuscular injection; the area should be gently massaged and, due to the possibility of vasomotor reactions, the patient should remain recumbent for 10 minutes and kept under close observation for 30 minutes after each injection. In the UK, 10 mg is given in the first week to test the patient's tolerance. If satisfactory, this may be followed by doses of 50 mg at weekly intervals until signs of remission occur; the dosage interval is then increased to 2 weeks until full remission occurs and then

increased gradually to every 4 to 6 weeks. Treatment may be continued for up to 5 years after remission.

Improvement may not be seen until a total dose of 300 to 500 mg has been given. If no major improvement has occurred after a total of 1 g has been given (excluding the test dose) therapy should be stopped; alternatively in the absence of toxicity, 100 mg may be given weekly for a further 6 weeks; should there be no response at this dose other forms of therapy should be tried. In patients who relapse while receiving maintenance therapy, the interval between doses should be reduced to one week and should not be increased again until control has been obtained; however, if no response is obtained within 2 months, alternative treatment should be used. It is important to avoid complete relapse since a second course of gold therapy is not usually effective.

For doses in juvenile idiopathic arthritis, see Administration in Children, below.

NSAIDs may be continued when sodium aurothiomalate therapy is begun.

Other gold compounds that have been used include auranofin (p.25), aurothioglucose (p.26), aurotioprol (p.26), gold keratinate (p.62), and sodium aurotiosulfate (below).

Administration in children. For children with progressive juvenile idiopathic arthritis the suggested initial weekly dose of sodium aurothiomalate is 1 mg/kg by deep intramuscular injection to a maximum of 50 mg weekly (one-tenth to one-fifth of the calculated initial weekly dose may be given for 2 to 3 weeks to test the patient's tolerance). Weekly doses should continue until signs of remission occur, at which point the dosage interval may be increased to fortnightly. With full remission, the dosage interval may again be increased gradually to every 4 weeks. If no improvement has occurred after 20 weeks, the dose could be raised slightly or another antirheumatic drug tried. For the view that use of gold compounds is no longer appropriate to treat juvenile idiopathic arthritis see Rheumatic Disorders, below.

Asthma. For comment on the use of parenteral gold compounds in the treatment of asthma, see under Auranofin, p.26.

Pemphigus and pemphigoid. Corticosteroids are the main treatment for blistering in pemphigus and pemphigoid (p.1582). Intramuscular gold therapy has been used concomitantly to permit a reduction in corticosteroid dosage although evidence for the steroid-sparing effect is lacking;[1,2] it has been suggested that gold therapy should be reserved for patients who cannot tolerate corticosteroids or in whom they are contra-indicated.[1]

1. Bystryn J-C, Steinman NM. The adjuvant therapy of pemphigus: an update. *Arch Dermatol* 1996; **132:** 203–12.
2. Pandya AG, Dyke C. Treatment of pemphigus with gold. *Arch Dermatol* 1998; **134:** 1104–7.

Rheumatic disorders. Gold compounds are among the disease-modifying antirheumatic drugs (DMARDs) that may be used in the treatment of rheumatoid arthritis (p.11). Although toxicity has now reduced its popularity, intramuscular gold has long been used for the treatment of rheumatoid arthritis[1-4] and is often the standard against which the efficacy of other treatments is measured. Oral gold is less toxic but is also much less effective. It is unclear if there are differences between available intramuscular forms, but a study[5] in 120 patients converted from aurothioglucose to aurothiomalate found that 29 withdrew from the latter drug within 12 months, mostly because of lack of efficacy or the development of adverse effects not seen with the previous drug.

Gold compounds have also been used in the treatment of juvenile idiopathic arthritis (p.10); however, the *BNFC* states that gold is no longer used for this indication.

Gold compounds may also be of benefit in psoriatic arthritis (see under Spondyloarthropathies, p.13).

1. Epstein WV, *et al.* Effect of parenterally administered gold therapy on the course of adult rheumatoid arthritis. *Ann Intern Med* 1991; **114:** 437–44.
2. Anonymous. Gold therapy in rheumatoid arthritis. *Lancet* 1991; **338:** 19–20.
3. Klinkhoff AV, Teufel A. How low can you go? Use of very low dosage of gold in patients with mucocutaneous reactions. *J Rheumatol* 1995; **22:** 1657–9.
4. Clark P, *et al.* Injectable gold for rheumatoid arthritis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 1997 (accessed 13/11/06).
5. van Roon, EN, *et al.* Parenteral gold preparations: efficacy and safety of therapy after switching from aurothioglucose to aurothiomalate. *J Rheumatol* 2005; **32:** 1026–30.

Preparations

BP 2008: Sodium Aurothiomalate Injection;
USP 31: Gold Sodium Thiomalate Injection.

Proprietary Preparations (details are given in Part 3)
Austral.: Myocrisin; ***Austria:*** Tauredon; ***Canad.:*** Myochrysine; ***Cz.:*** Tauredon; ***Denm.:*** Myocrisin; ***Fin.:*** Myocrisin; ***Ger.:*** Tauredon; ***Gr.:*** Miocrin; Myocrysine†; Tauredon; Tuaredon†; ***Hung.:*** Tauredon†; ***Irl.:*** Myocrisin; ***Neth.:*** Tauredon; ***Norw.:*** Myocrisin; ***NZ:*** Myocrisin; ***Port.:*** Tauredon; ***S.Afr.:*** Myocrisin†; ***Singapore:*** Miocrin; ***Spain:*** Miocrin; ***Swed.:*** Myocrisin; ***Switz.:*** Tauredon; ***Thai.:*** Myocrisin; ***UK:*** Myocrisin; ***USA:*** Aurolate; Myochrysine.

Sodium Aurotiosulfate *(rINN)*

Aurotiosulfate de Sodium; Aurotiosulfato de sodio; Gold Sodium Thiosulphate; Natrii Aurotiosulfas; Natrii Aurotiosulphas; Natriumaurotiosulfaatti; Natriumaurotiosulfat; Sodium Aurothiosulphate; Sodium Dithiosulfatoaurate.

Натрия Ауротиосульфат

$Na_3Au(S_2O_3)_2,2H_2O$ = 526.2.

CAS — 10233-88-2 (anhydrous sodium aurotiosulfate); 10210-36-3 (sodium aurotiosulfate dihydrate).
ATC — M01CB02.
ATC Vet — QM01CB02.

Profile

Sodium aurotiosulfate has a gold content of about 37%. It has similar actions and uses to those of sodium aurothiomalate (p.122). It is given by intramuscular injection in a usual dose of 56.1 mg every 5 to 7 days.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Crytion; ***Chile:*** Crytioro; ***Ital.:*** Fosfocrisolo.

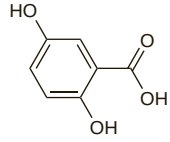
Sodium Gentisate *(rINN)*

Gentisate de Sodium; Gentisato de sodio; Gentisato Sodico; Natrii Gentisas. Sodium 2,5-dihydroxybenzoate dihydrate.

Натрия Гентизат

$C_7H_5NaO_4,2H_2O$ = 212.1.

CAS — 490-79-9 (gentisic acid); 4955-90-2 (anhydrous sodium gentisate).



(gentisic acid)

Pharmacopoeias. In *Fr.*

Profile

Sodium gentisate has been used as an analgesic in the treatment of musculoskeletal and joint disorders. It is also used as a preservative.

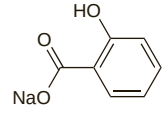
Sodium Salicylate

Natrii salicylas; Natrio salicilatas; Natriumsalicylat; Natriumsalisylaatti; Nátrium-szalicilát; Salicilato sódico; Salicylan sodný; Sodium, salicylate de; Sodu salicylan; Sodyum Salisilat. Sodium 2-hydroxybenzoate.

Салицилат Натрия

$C_7H_5NaO_3$ = 160.1.

CAS — 54-21-7.
ATC — N02BA04.
ATC Vet — QN02BA04.



Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Sodium Salicylate). Colourless small crystals or shiny flakes, or white or almost white, crystalline powder. Freely soluble in water; sparingly soluble in alcohol. Store in airtight containers. Protect from light.

USP 31 (Sodium Salicylate). Amorphous or microcrystalline powder or scales. It is colourless or has not more than a faint pink tinge. It is odourless or has a faint characteristic odour. A freshly made 10% solution in water is neutral or acid to litmus. Freely (and slowly) soluble in water and in glycerol; very soluble in boiling water and in boiling alcohol; slowly soluble in alcohol. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Aspirin, p.20.

Although sodium salicylate has been used in the treatment of rheumatic fever, its high sodium content may cause problems in patients with cardiac complications.

The use of aspirin and other acetylated salicylates is generally not recommended for children because of the risk of Reye's syndrome, unless specifically indicated. Some licensed drug information extends this precaution to sodium salicylate.

Effects on the eyes. Retinal haemorrhages were reported in a 60-year-old woman taking sodium salicylate 6 g daily by mouth for 2 months and in a 10-year-old girl taking sodium salicylate, 4 g daily by mouth, for 40 days.[1] In both cases the haemorrhages gradually resolved after the treatment was stopped.

1. Mortada A, Abboud I. Retinal haemorrhages after prolonged use of salicylates. *Br J Ophthalmol* 1973; **57:** 199–200.

Interactions

For interactions associated with salicylates, see Aspirin, p.23.

Uses and Administration

Sodium salicylate is a salicylic acid derivative that has analgesic, anti-inflammatory, and antipyretic actions similar to those of aspirin (p.23). Sodium salicylate 1 g is equivalent to about 1.1 g of aspirin. It is used in the treatment of pain, fever, and in rheumatic disorders such as osteoarthritis and rheumatoid arthritis. The usual oral dose of sodium salicylate for pain or fever is 325 to 650 mg every four hours as required. The oral dose for rheumatic disorders is 3.6 to 5.4 g daily in divided doses. Sodium salicylate has also been used in the symptomatic treatment of rheumatic fever but its high sodium content may cause problems in patients with cardiac complications.

Sodium salicylate has also been given by intravenous infusion and topically.

Preparations

USP 31: Sodium Salicylate Tablets.

Proprietary Preparations (details are given in Part 3)
Canad.: Dodds†; Saliject; ***NZ:*** Hairscience Shampoo†; ***Turk.:*** Enter-Sal; ***UK:*** Jackson's Pain & Fever.

Multi-ingredient: ***Braz.:*** A Saude da Mulher; Abacateirol†; Pilulas De Witt's†; ***Canad.:*** Plax; Thunas Tab for Menstrual Pain†; ***Chile:*** Eucerin Shampoo Anticaspa; ***Fr.:*** Brulex; ***Ger.:*** Gelonida NA†; ***Hong Kong:*** Gly Thymol; ***S.Afr.:*** Colphen; Doans Backache Pills; Ilvico; TCP; ***UK:*** Antiseptic Mouthwash; Doans Backache Pills; TCP; ***USA:*** Cystex; Scot-Tussin Original 5-Action; Tussirex; ***Venez.:*** Boncilin†; Inquilim†.

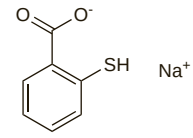
Sodium Thiosalicylate

Tiosalicilato sódico. Sodium 2-sulfanylbenzoate.

Тиосалицилат Натрия

$C_7H_5O_2NaS$ = 176.2.

CAS — 134-23-6.



Profile

Sodium thiosalicylate is a salicylic acid derivative (see Aspirin, p.20) that has been used parenterally in the treatment of musculoskeletal disorders, osteoarthritis, rheumatic fever, and acute gout.

Preparations

Proprietary Preparations (details are given in Part 3)
USA: Rexolate†.

Sufentanil *(BAN, rINN)* ⊗

R-30730; Sufentaniili; Sufentanilis; Sufentanilo; Sufentanilum; Szufentanil. *N*-{4-(Methoxymethyl)-1-[2-(2-thienyl)ethyl]-4-piperidyl}propionanilide.

Суфентанил

$C_{22}H_{30}N_2O_2S$ = 386.6.

CAS — 56030-54-7.
ATC — N01AH03.
ATC Vet — QN01AH03.