Preparations

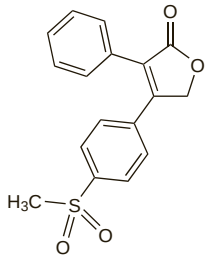
Proprietary Preparations (details are given in Part 3)
Arg.: Remicit; Ultiva; ***Austral.:*** Ultiva; ***Austria:*** Ultiva; ***Belg.:*** Ultiva; ***Braz.:*** Ultiva; ***Canad.:*** Ultiva; ***Chile:*** Ultiva; ***Cz.:*** Ultiva; ***Denm.:*** Ultiva; ***Fin.:*** Ultiva; ***Fr.:*** Ultiva; ***Ger.:*** Ultiva; ***Gr.:*** Ultiva; ***Hong Kong:*** Ultiva; ***Hung.:*** Ultiva†; ***Irl.:*** Ultiva†; ***Israel:*** Ultiva; ***Ital.:*** Ultiva; ***Mex.:*** Ultiva; ***Neth.:*** Ultiva; ***Norw.:*** Ultiva; ***NZ:*** Ultiva; ***Pol.:*** Ultiva; ***Port.:*** Ultiva; ***S.Afr.:*** Ultiva; ***Singapore:*** Ultiva; ***Spain:*** Ultiva; ***Swed.:*** Ultiva; ***Switz.:*** Ultiva; ***Turk.:*** Ultiva; ***UK:*** Ultiva; ***USA:*** Ultiva; ***Venez.:*** Ultiva.

Rofecoxib *(BAN, USAN, rINN)*

MK-966; MK-0966; Rofécoxib; Rofecoxibum; Rofekoksibi; Rofekoxib. 4-[*p*-(Methylsulfonyl)phenyl]-3-phenyl-2(5*H*)-furanone.

Рофекоксиб

$C_{17}H_{14}O_4S$ = 314.4.
CAS — 162011-90-7.
ATC — M01AH02.
ATC Vet — QM01AH02.



Profile

Rofecoxib is an NSAID (p.96) reported to be a selective inhibitor of cyclo-oxygenase-2 (COX-2). It was given orally for symptomatic relief in the treatment of osteoarthritis and rheumatoid arthritis, and in the management of acute pain, dysmenorrhoea, and migraine but was generally withdrawn worldwide after reports of cardiovascular adverse effects (see below).

Rofecoxib has been applied topically in some countries.

Effects on the cardiovascular system. As of February 2001, the UK CSM had received a small number of reports of *myocardial infarction* or *ischaemia* associated with the selective cyclo-oxygenase-2 (COX-2) inhibitors.[1] At that time it noted that COX-2 inhibitors such as rofecoxib did not possess the intrinsic antiplatelet activity associated with aspirin, and consequently did not provide protection against ischaemic cardiac events. Data from a large, randomised study also showed the incidence of myocardial infarction to be greater in patients taking rofecoxib than in those taking naproxen.[2] Postmarketing surveillance of rofecoxib continued to provide further case reports of adverse cardiovascular effects. In addition, results of the then unpublished APPROVe study of rofecoxib for prevention of adenomatous polyposis indicated that the risk of myocardial infarction and stroke was markedly increased in patients receiving the drug compared to those on placebo; however, this difference was only apparent after 18 months of treatment. As a result, the study was stopped early and, in September 2004, the manufacturer generally withdrew rofecoxib worldwide. The cardiovascular findings from the APPROVe study were published in 2005;[3] the results showed a twofold increase in the risk of adverse cardiovascular events in patients receiving rofecoxib 25 mg daily when compared with those on placebo. More recently, 1-year follow-up data for patients in the APPROVe study has been released. In a statement from the manufacturer,[4] it is noted that in the year after rofecoxib was stopped there was no statistically significant difference in the risk of confirmed thrombotic cardiovascular events in those patients who had previously taken rofecoxib compared with those who had been given placebo; however, when data from both the on- and off-treatment periods were considered together, the difference in the risk of cardiovascular events between the rofecoxib and the placebo groups remained significant. Combined data from the on- and off-treatment periods also showed that there was an increased risk of confirmed heart attacks and ischaemic strokes in the rofecoxib group when compared to the placebo group. (The data for ischaemic stroke were later published.[5]) Similar data, suggesting a 1.5-fold increase in risk of thrombotic events with rofecoxib, were reported from a study of adjuvant use for colorectal cancer.[6] A cumulative meta-analysis also indicated an increased risk of myocardial infarction in patients receiving rofecoxib.[7]

Subsequent investigation by US and European regulatory authorities has confirmed that other COX-2 inhibitors are also associated with some increased cardiovascular risk (see under Celecoxib, p.34), as are some non-selective NSAIDs (see Thrombotic Events, p.97).

A review[8] of prospective studies evaluating the effect of selective COX-2 inhibitors on blood pressure was unable to determine if there was any association between the use of these drugs and blood pressure elevations. Of the studies considered, a randomised study in elderly, hypertensive patients with osteoarthritis has suggested that the risk of developing *increased systolic blood pressure* is greater in those patients receiving rofecoxib than in those receiving celecoxib.[9] However, the manufacturers of rofecoxib have pointed out that the trial used doses of rofecoxib greater than those recommended for elderly or hypertensive patients.

1. CSM/MCA. COX-2 selective NSAIDs lack antiplatelet activity. *Current Problems* 2001; **27:** 7. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007458&RevisionSelectionMethod=LatestReleased (accessed 08/11/07)
2. Bombardier C, *et al.* Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. *N Engl J Med* 2000; **343:** 1520–8.
3. Bresalier RS, *et al.* Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. *N Engl J Med* 2005; **352:** 1092–1102. Correction. *ibid.* 2006; **355:** 221.
4. Merck, USA. Merck announces preliminary analyses of off-drug extension of APPROVe study (issued 11th May, 2006). Available at: http://www.merck.com/newsroom/press_releases/corporate/2006_0511.html (accessed 08/11/07)
5. Afilalo J, *et al.* Long-term risk of ischemic stroke associated with rofecoxib. *Cardiovasc Drugs Ther* 2007; **21:** 117–20.
6. Kerr DJ, *et al.* Rofecoxib and cardiovascular adverse events in adjuvant treatment of colorectal cancer. *N Engl J Med* 2007; **357:** 360–9.
7. Jüni P, *et al.* Risk of cardiovascular events and rofecoxib: cumulative meta-analysis. *Lancet* 2004; **364:** 2021–9.
8. Johnson DL, *et al.* Effect of cyclooxygenase-2 inhibitors on blood pressure. *Ann Pharmacother* 2003; **37:** 442–6.
9. Whelton A, *et al.* Cyclooxygenase-2-specific inhibitors and cardiorenal function: a randomized, controlled trial of celecoxib and rofecoxib in older hypertensive osteoarthritis patients. *Am J Ther* 2001; **8:** 85–95.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Antidol†; Blokium Cox†; Coxiro†; Foldoxx†; Toloxane†; Vioxx†; ***Austral.:*** Vioxx†; ***Austria:*** Ceoxx†; Coxxil†; Vioxx†; ***Belg.:*** Vioxx†; ***Braz.:*** Vioxx†; ***Canad.:*** Vioxx†; ***Chile:*** Ceoxx†; ***Cz.:*** Vioxx†; ***Denm.:*** Vioxx†; Vioxxalt†; ***Fin.:*** Vioxx†; ***Fr.:*** Vioxx†; ***Ger.:*** Vioxx†; ***Gr.:*** Peroxx†; Vioxx†; ***Hong Kong:*** Vioxx†; ***Hung.:*** Vioxx†; ***India:*** Alrof†; Dolib†; Rofetab†; Rofib; Rofixx†; Rofiz; Versatil†; ***Irl.:*** Ceoxx†; Vioxx†; ***Israel:*** Vioxx†; ***Ital.:*** Arofexx†; Coxxil†; Dolcoxx†; Dolostop†; Miraxx†; Vioxx†; ***Malaysia:*** Vioxx†; ***Mex.:*** Vioxx†; ***Neth.:*** Vioxx†; ***Norw.:*** Vioxx†; ***NZ:*** Vioxx†; ***Port.:*** Ceoxx†; Coxxil†; Vioxx†; ***S.Afr.:*** Vioxx†; ***Singapore:*** Vioxx†; ***Spain:*** Ceoxx†; Vioxx†; ***Swed.:*** Vioxx†; Vioxxakut†; ***Switz.:*** Vioxx†; ***Thai.:*** Vioxx†; ***UK:*** Vioxx†; ***USA:*** Vioxx†; ***Venez.:*** Vioxx†.

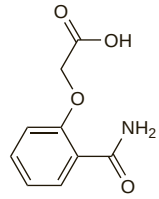
Multi-ingredient: ***India:*** Rofecip Plus†.

Salamidacetic Acid

Carbamoylphenoxyacetic acid; Salamidacético, ácido; Salicylamide *O*-acetic acid. (2-Carbamoylphenoxy)acetic acid.

Натрия Салициламидацетат (sodium salamidacetate)

$C_9H_9NO_4$ = 195.2.
CAS — 25395-22-6 (salamidacetic acid); 3785-32-8 (sodium salamidacetate).



Profile

Salamidacetic acid is a salicylic acid derivative (see Aspirin, p.20) that has also been used as the sodium and diethylamine salts for the treatment of musculoskeletal and joint disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Akistin; ***Ger.:*** Clinit N†.

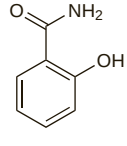
Multi-ingredient: ***Austria:*** Ambene; Rheumesser; ***Ger.:*** Caye Rheuma-Balsam; ***Rus.:*** Ambene (Амбене); ***Thai.:*** Trabit†.

Salicylamide *(BAN, rINN)*

Salicilamida; Salicylamid; Salicylamidum; Salisyyliamidi. 2-Hydroxybenzamide.

Салициламид

$C_7H_7NO_2$ = 137.1.
CAS — 65-45-2.
ATC — N02BA05.
ATC Vet — QN02BA05.



Pharmacopoeias.

In *Pol.* and *US.*

USP 31 (Salicylamide). A white practically odourless crystalline powder. Slightly soluble in water and in chloroform; soluble in alcohol and in propylene glycol; freely soluble in ether and in solutions of alkalis.

Profile

Salicylamide is a salicylic acid derivative (see Aspirin, p.20) but is not hydrolysed to salicylate; it is almost completely metabolised to inactive metabolites during absorption and on first pass through the liver. It is given in usual oral doses of 325 to 650 mg or more, usually with other analgesics, three or four times daily for pain and fever. Salicylamide has also been applied topically in rubefacient preparations in concentrations of up to about 5% for the relief of muscular and rheumatic pain.

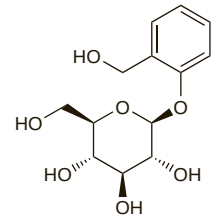
Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Waldheim Rheuma-Creme.

Multi-ingredient: ***Arg.:*** Finagrip†; Funciogrip; Venter; ***Austria:*** Rilfit; Rubriment; Sigmalin B ; Sigmalin B forte; Sigmalin B ohne Coffein; Spalt†; Waldheim Influvidon; Waldheim Sport- und Rheuma-Fluid; ***Belg.:*** Percutalgine; ***Braz.:*** Coristina R; Nogripe; Resprax; Termogripe C†; Vita Grip; ***Denm.:*** Kodamid; Koffisal; ***Fr.:*** Percutalgine; ***Ger.:*** Glutisal†; Salistoperm†; ***Gr.:*** Myalgesic†; ***Hong Kong:*** Antiflu Forte; Antiflu-N-Forte; DF Multi-Symptom; Flu-Zep; Neozep; Qualizep; ***Indon.:*** Cold Cap; Corexin; Neozep; Refagan; ***Ital.:*** Anticorizza†; ***Mex.:*** Artrilan; Butayonacol; ***NZ:*** Calm-U; ***Pol.:*** Reumosol; Scorbolamid; ***Rus.:*** Cefecon N (Цефекон Н); Percutalgine (Перкуталжин)†; ***S.Afr.:*** Colcaps; Flutex Cold and Flu; Histamed Compound; Ilvico; Specific Nerve Pain Remedy; ***Spain:*** Coricidin†; Hubergrip†; Pridio; Rinomicine; Rinomicine Activada; Yendol; ***Switz.:*** Escalgin sans codeine†; Escognipp sans codeine; Grippalgine N†; Osa Gel de dentition; ***Thai.:*** Apracur; Fecol; Percutalgine†; ***UAE:*** Adol Compound; Flukit; ***UK:*** Intralgin†; ***USA:*** Anabar; BC; Be-Flex Plus; By-Ache; Combiflex; Duraxin; Levacet; Lobac; Painaid; Saleto; Stanback Headache; Trim-Elim†; ***Venez.:*** Cotar†; Praxona.

Salix

Corteza de sauce; Écorce de Saule; Fűzfakéreg; Gluosnių žievė; Kora wierzby; Pajunkuori; Sälgbark; Salicis cortex; Saule, écorce de; Vrbová kůra; Weidenbaumrinde; White Willow Bark; Willow Bark.



(salicin)

Pharmacopoeias.

In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Willow Bark). The whole or fragmented dried bark of young branches or whole dried pieces of current year twigs of various species of the genus *Salix*, including *Salix purpurea*, *S. daphnoides*, and *S. fragilis*. It contains not less than 1.5% of total salicylic derivatives, expressed as salicin ($C_{13}H_{18}O_7$ = 286.3), calculated with reference to the dried drug. Protect from light.

Profile

Salix contains variable amounts of tannin and also of salicin, which has antipyretic and analgesic actions similar to those of aspirin. Salix has been used in a variety of herbal remedies for painful and inflammatory conditions and for fever. It was once used as a bitter.

Adverse effects. An *anaphylactic reaction* developed in a 25-year-old woman with asthma and a known allergy to aspirin, within 75 minutes of ingesting a dietary supplement containing willow bark extract.[1] The link between salicylate and willow bark allergy was also reported in a carpenter who experienced a widespread *rash*, similar to that he developed with aspirin, when working with willow wood.[2]

1. Boullata JI, *et al.* Anaphylactic reaction to a dietary supplement containing willow bark. *Ann Pharmacother* 2003; **37:** 832–5.
2. Jennings A. Link between salicylate and willow bark. *Pharm J* 2006; **276:** 417.

Pain. Preparations containing willow bark extract have been tried with some success in the treatment of musculoskeletal disorders such as low back pain[1-3] and osteoarthritis.[4] However, the quality of reporting in trials is generally poor and further studies are needed to establish their place in therapy.

1. Chrubasik S, *et al.* Treatment of low back pain exacerbations with willow bark extract: a randomized double-blind study. *Am J Med* 2000; **109:** 9–14.

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

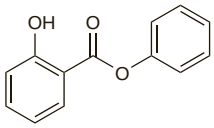
Proprietary Preparations (details are given in Part 3)
Braz.: Zortrix; ***Ger.:*** Assalix; Assplant; Lintia†; Rheumakaps; Rheumatab Salicis†; ***Pol.:*** Salicortex; ***Switz.:*** Assalix.

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.

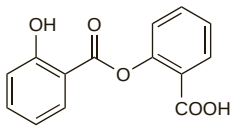
Multi-ingredient: ***Arg.:*** Dermithan; ***Austria:*** Carl Baders Divinal; ***Belg.:*** Borostyrol; ***Braz.:*** Talco Alivio†; ***Canad.:*** Franzbranns†; ***Chile:*** Galutec†; Polisep†; ***Cz.:*** Parodontal F5†; ***Fr.:*** Borostyrol; Dermophil Indien†; Nisacalm; ***Pol.:*** Salotannal; Urosal; ***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

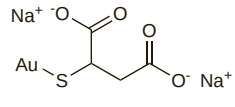
Proprietary Preparations (details are given in Part 3)
USA: Sarapin.

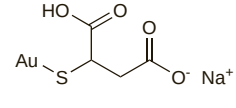
Sodium Aurothiomalate *(rINN)*

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-