Sodium aurothiomalate (i.m gold) for rheumatoid arthritis and other rheumatological diseases (Adults)

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).
This guideline reinforces the basic premise that:
When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the "sharing of information with the individual GP and their mutual agreement to the transfer of care."
These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Indications:	**Dosage and administration:**
Sodium aurothiomalate (gold) is used in the management of active progressive rheumatoid arthritis	Given by deep intramuscular injection. Test dose 10 mg must be given in clinic followed by 30 mins observation to look for signs of allergic reaction, followed by 50 mg once weekly until there is definite evidence of remission, then reduced to 50 mg every 4 weeks continued for up to 5 years after complete remission, dose to be reduced gradually. Benefit is not expected until 300–500 mg has been given; it should be discontinued if there is no remission after 1 g has been given and alternative DMARD therapy considered ***Relapse in patients who have previously received sodium aurothiomalate*** By deep intramuscular injection 50 mg once weekly until control has been obtained again, then reduced to 50 mg every 4 weeks continued for up to 5 years after complete remission, if no response is seen within 2 months, alternative treatment should be sought Dosing in renal impairment: CrCl <50-80ml/min: use with caution CrCl <50ml/min: avoid use

Additional Information

- If anaphylactoid effects are observed, treatment should be discontinued.
    - Patients should be advised to seek prompt medical attention if diarrhoea, sore throat, fever, infection, non-specific illness, unexplained bleeding and bruising, purpura, mouth ulcers, metallic taste, rash, breathlessness, or cough develop.

Monitoring requirements:

Before treatment:

- Full blood count (FBC) including platelets, total and differential white cell count; urea and electrolyes (U&Es); creatinine and liver function tests (LFTs)
- Urinalysis

During treatment:

- FBC (including total and differential white cell and platelet counts) and urinalysis prior to each injection
- Patient should be asked about a rash (usually itchy) or oral ulceration prior to each injection
- U&Es, creatinine, LFTs 6 monthly.
- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio) and chest x ray (to monitor pulmonary fibrosis)
- ESR monthly for disease monitoring purposes

Responsibility for monitoring, once stable, rests with the GP

Provided blood results are stable, the results of the FBC need not be available before the injection is given but must be available before the next injection, i.e. it is permissible to work one FBC in arrears. Urinalysis should be carried out just before each injection.

Action to be taken if abnormal results/adverse effects:

- WBC< 3.5 x 10^9/l Check neutrophil count
- Neutrophils < 2.0 x 10^9/l Monitor weekly. If it falls below 1.5 x 10^9/l STOP DRUG and contact helpline.
- Platelets < 150 x 10^9/l Monitor weekly. If drop below 100 x 10^9/l contact helpline
- Eosinophils >0.5 x 10^9/l Monitor weekly, if persistent STOP DRUG and contact helpline
- Proteinuria 1+ or more Check MSSU: if infection present treat appropriately. If sterile and 1+ proteinuria or more persists, withhold until discussed with specialist team. STOP DRUG is presence of unexplained proteinuria (associated with immune complex nephritis) which is repeatedly above 300 mg/litre
- Rash/pruritis STOP DRUG and contact helpline
- Oral ulceration Repeat FBC and act on results as above
  Mild: salt water mouth wash
  Moderate: Hydrocortisone (Corlan) pellets (1 applied to affected area qds)
  Severe: Hydrocortisone (Corlan) pellets and contact helpline
- Abnormal bruising Repeat FBC and act on results as above
- Sore throat Repeat FBC and act on results as above
- Diarrhoea (very rare) STOP DRUG and contact helpline
- Gastrointestinal bleeding (associated with ulcerative enterocolitis) STOP DRUG

Please note that in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Contraindications:

- Sodium aurothiomalate (gold) should not be given to women who are pregnant, or likely to become pregnant without a careful assessment of risk versus benefit.
- Breastfeeding
- Severe renal or hepatic disease
- History of blood disorders or bone marrow aplasia
- Exfoliative dermatitis
- Systemic lupus erythematosus.
- Necrotising enterocolitis
- Pulmonary fibrosis
- Acute porphyria
- Live vaccines are contra-indicated in patients with impaired immune response.

Drug interactions: see appendix 1 of current BNF before co-prescribing any drugs

- Penicillamine- increased risk of haematological toxicity
- Caution if phenylbutazone or oxyphenbutazone are administered concurrently
- Concurrent gold administration may exacerbate aspirin-induced hepatic dysfunction
- Avoid concomitant use of ACE inhibitors – increased risk of severe anaphylactoid reaction, flushing and hypotension (potentially severe) reported when sodium aurothiomalate given with ACE inhibitors

Cautions:

- Elderly
- Patients with a history of urticaria, eczema or inflammatory bowel disease.
- Mild to moderate renal impairment, pre-existing proetinuria
- Mild to moderate hepatic impairment
- Patients should be advised to minimise exposure to ultraviolet light to avoid irreversible skin pigmentation in sun exposed area

Adverse Effects:

Blood disorders, GI bleeding, severe anaphylactic reactions, stomatitis, taste disturbances, colitis, hepatotoxicity with cholestatic jaundice, pulmonary fibrosis, peripheral neuropathy, mouth ulcers, proteinuria, nephrotic syndrome, gold deposits in the eye, alopecia, skin reactions (including, on prolonged parenteral treatment, irreversible pigmentation in sun exposed areas).

Specialist responsibilities:

- Confirm the diagnosis of rheumatoid arthritis
- Discuss with the patient the benefits and side effects of treatment with sodium aurothiomalate (gold).
- If the patient is a woman of child bearing potential – ensure that they are aware of the importance of effective contraception and the need to discuss with their consultant if they wish to become pregnant
- Ensure that the patient understands and accepts their responsibilities (see section below)
- Seek consent for treatment and document in the patient's notes.
- Ensure baseline monitoring of full blood count and biochemical profile
- Discuss how the patient/carer can be aware of possible signs of sodium aurothiomalate (gold) toxicity or intolerance
- Provide written instruction to the GP for initiation and escalation of sodium aurothiomalate (gold).
- Provide the patient with a shared care booklet and enter the blood results into the booklet.
- Review the patient at the intervals specified above to monitor the patient's disease activity, the efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
- Discontinue if no response or patient has a significant adverse effect.
- Promptly communicate with the GP via a clinic letter any changes in treatment, results of monitoring undertaken, and assessment of adverse events. The clinic letter should clearly state if the dose has remained the same or if a dose adjustment had been made – specifically highlighting the new dose in comparison with the preceding one.
- Advise GPs when to stop treatment.
- Provide clear arrangements for back-up, advice and support.
- Report serious adverse events to the Medicines and Health Regulatory Agency (MHRA) at https://yellowcard.mhra.gov.uk/

GP's responsibilities:

- Initial referral to Consultant Rheumatologist raising the possibility of rheumatoid arthritis
- Following the initial dose (given in the hospital) prescribe sodium aurothiomalate and administer following written instructions for escalation by the specialist.
- Continue monitoring as outlined on the first page and document the results in the shared care booklet.
- Ensure patient's shared care booklet and practice computer system are updated with any dose changes.
- Refer promptly to the specialist if there is a change in the patient's status or concerns regarding compliance. In most cases, do not stop treatment without discussion with the Rheumatology Helpline.
- If patient fails to attend more than 2 monitoring visits it is not safe to continue treatment – contact the Rheumatology Helpline for advice.
- Report serious adverse events to the specialist and MHRA https at https://yellowcard.mhra.gov.uk/
- Administer Pneumococcal Vaccine/ Pneumovax® II and annual influenza vaccines.
- Consider passive immunisation with Varicella zoster immunoglobulin in non-immune patients exposed to chicken pox or shingles.

Patient responsibilities:

- Read the written patient information provided about the drug and have a clear understanding of the risks/benefits of sodium aurothiomalate (gold) treatment.
- Attend for blood tests.
- Report any adverse effects to their GP and/or specialist whilst treated with sodium aurothiomalate (gold).
- Limit alcohol to national safe weekly limits
- Take monitoring booklet every time the patient sees the GP, has a hospital appointment or visits the pharmacist.

Secondary care review: During initiation: 4 – 6 weekly until controlled
Once disease controlled: Annual review by consultant

Availability: 10mg/0·5ml x 10 ampoules = £45.55, 50mg/0·5ml x 10 ampoules = £134.80 (Brand name: Myocrisin)
Prices correct at time of writing, online MIMS March 2016

Back up advice and support: Rheumatology Helpline	**Telephone:** 0151 604 7505

Written By:	Rachael Pugh, Prescribing Adviser, Paul Wallace Practice Pharmacist, Abigail Cowan, Prescribing Adviser, Wirral Medicines Management Team (MLCSU)	Dr Geraldine M^{c}Caffrey, Lead Pharmacist, Division of Medical Specialties and Acute Care, WUTH Dr Yee Ho Chiu, Consultant Rheumatologist, WUTH Dr Mano George, Consultant Rheumatologist, WUTH