PRODUCT INFORMATION
MYOCRISIN®

NAME OF THE MEDICINE

Non-proprietary Name
Sodium aurothiomalate

DESCRIPTION
Each ampoule of MYOCRISIN solution for injection contains 10mg, 20mg or 50mg of sodium aurothiomalate and phenylmercuric nitrate and water for injections.

PHARMACOLOGY

Site and Mode of Action
In rheumatoid arthritis, MYOCRISIN appears to suppress the disease processes in two ways. Firstly it penetrates into the joint cavity and affects the lysosomal membranes. Secondly, it binds to plasma proteins, including IgG, the rheumatoid factor and the immune complex so that when the lysosomes ingest immune complex the gold is absorbed with it and inactivates lysosomal enzymes within the cell.

INDICATIONS
Adjunctive treatment of rheumatoid arthritis that is not adequately controlled by other anti-inflammatory agents and conservative measures. In chronic, advanced cases of rheumatoid arthritis, gold therapy is less valuable.

Still's disease.

CONTRAINDICATIONS
Hypersensitivity to any component of this product. Patients with gross renal or hepatic disease, diabetes, marked toxaemia, a history of blood dyscrasias or exfoliative dermatitis.

Use in Pregnancy is contraindicated (See Precautions).

PRECAUTIONS
Every candidate for gold therapy should be investigated fully to prevent the administration of gold to those with gross renal or hepatic defects, diabetes, marked toxaemia, a history of blood dyscrasias or dermatitis. Before starting treatment, and again before each injection, the urine should be tested for protein, the skin inspected for rashes, and a full blood count performed, with a numerical platelet count (not an estimation). The availability, whenever possible, of the results of blood counts before the next injection is a useful aid in minimising toxic reactions. Minimum values below which gold should not be given until the count has been repeated and there is return to normal values are: total white cells 4,000/mm³, neutrophils 2,000/mm³, platelets 150,000/mm³. It is unwise to continue with gold injections when there is a persistent or otherwise unexplained eosinophilia exceeding 1,000/mm³, as this may indicate an impending toxic reaction. Particular vigilance should be maintained during the period when between 300 to 500mg of gold has been given because it is at this time that a blood dyscrasia is most likely to occur.

If the full blood count is normal after the cumulative gold dose reaches 500mg, and provided the full blood count remains normal, full blood counts can be done before every second injection. The presence of proteinuria, pruritus, or rash, or an eosinophilia are indications of developing toxicity; the dose of MYOCRISIN should be withheld for one to two weeks until all signs have disappeared, when the treatment may be restarted on a smaller dosage.
MYOCRISIN may be given in the presence of a trace of protein, but if there is 30mg/100mL or more, in the absence of urinary infection or other cause it may indicate a developing gold nephropathy and the treatment should be stopped.

Generally, this induces a complete reversal although in some instances the proteinuria may persist for many months.

The complaint of metallic taste, sore throat, glossitis, buccal ulceration and or easy bruising or bleeding demands an immediate blood count, followed, if indicated, by appropriate treatment for agranulocytosis and or thrombocytopenia. All patients receiving the drug should be warned both verbally and in writing to report immediately the appearance of sore throat, mouth or tongue, or the development of bruising or unusual bleeding.

As gold preparations cause ocular adverse effects, ophthalmological examination is recommended if ocular symptoms occur.

MYOCRISIN should be used with care in patients with marked hypertension or compromised cerebral or cardiovascular circulation.

As with other gold preparations, reactions which resemble anaphylactoid effects have been reported. These effects may occur after any course of therapy within the first 10 minutes following drug administration (see Dosage and Administration). If anaphylactoid effects are observed, treatment with MYOCRISIN should be discontinued.

Use in Pregnancy

Category B2

Like other heavy metals, gold may pass the placental barrier and may cause foetal damage; therefore, it should not be given during pregnancy, but as rheumatoid arthritis usually shows an improvement at this time, the withdrawal of gold is more than justifiable.

Use in Lactation

The presence of gold has been demonstrated in the milk of lactating mothers and in the serum and red blood cells. The use of MYOCRISIN for nursing mothers is not recommended.

Interactions with other Medicines

Gold salts should not be used concomitantly with penicillamine.

Extra caution should be exercised if phenylbutazone or oxyphenbutazone are administered concurrently.

Gold administration may exacerbate aspirin induced hepatic dysfunction.

Caution is needed in patients treated concomitantly with sodium aurothiomalate and angiotensin-converting enzyme inhibitors due to an increased risk of severe anaphylactoid reactions in these patients.

ADVERSE EFFECTS

These appear to be associated with individual tolerance, and may be largely avoided by careful titration of dosage. Skin rashes are frequent and commonly benign, but as such reactions may be the forerunners of severe gold toxicity, they must never be treated lightly. Skin complications include pruritus, erythema and transient eczema. Proteinuria is less common and indicates caution, but heavy proteinuria is a sign of more serious nephritis such as nephrotic syndrome or glomerulonephritis.

There have been some reports of gold deposits in the lens or cornea of patients treated with gold. These deposits have not led to any eye disorders or any degree of visual impairment, and have cleared within 3-6 months of cessation of therapy.

Haematuria may also develop. The most severe reactions due to gold are agranulocytosis, thrombocytopenia or aplastic anaemia; these occur usually in sensitive patients when a total of about 300mg has been given.
Stomatitis and oral mucous membrane reactions (such as ulcers) have been observed. Reactions of the "nitroid type" which may resemble anaphylactoid effects have been reported. Flushing, fainting, dizziness and sweating are most frequently reported.

Neurological manifestations of gold toxicity including very rare cases of peripheral neuropathy, Guillain-Barré syndrome and encephalopathy have been observed.

Other Reactions Include:
Gastrointestinal reactions such as nausea, vomiting, anorexia, abdominal cramps, diarrhoea, ulcerative enterocolitis; reactions involving the eye such as iritis, corneal ulcers, gold deposits in ocular tissues; peripheral neuropathy, elevated spinal fluid protein; CNS complications including confusion, hallucinations and seizures; hepatitis; jaundice; gold bronchitis; pulmonary injury manifested by interstitial pneumonitis and fibrosis; alopecia; fever; arthralgia.

Treatment with MYOCRISIN should be discontinued immediately when toxic reactions occur.
MYOCRISIN should not be reinstated after severe or idiosyncratic reactions.

**DOSAGE AND ADMINISTRATION**
MYOCRISIN should be administered only by intramuscular injection.

Because of the possibility of an anaphylactic reaction, it is recommended that patients be kept under medical observation for a period of 30 minutes after the administration of the drug.

Do not use a darkened solution (more than pale yellow).

**Rheumatoid arthritis**
Dosage should be adjusted according to the response of the patient. Recommended initial dosage schedules: injection, at weekly intervals, of 1, 5 and 10mg to test the patient's tolerance, followed by a 50mg/week to a total of 1g, or twenty weekly injections of 50mg to a total of 1g. Whatever initial dosage regimen is adopted it is essential to continue therapy on a maintenance basis, usually at the rate of 50mg/month until a total of about 3g has been given; alternatively, the treatment is continued indefinitely or maintained for at least two years after remission has been achieved.

**Still's disease**
Dosage is proportionate to the body weight of the patient. MYOCRISIN is given at weekly intervals, initiating treatment with the smallest doses and increasing to the following maxima: under 25kg bodyweight: 10mg; 25 to 50kg bodyweight: 20mg; over 50kg bodyweight: 50mg.

Therapy should be continued for about six months. If at this time there is no improvement the gold is stopped, but in cases showing improvement, maintenance therapy with fortnightly or monthly injections of the previous dosage should be given for one to five years.

**OVERDOSAGE**
The appearance of side effects indicates that the individual is receiving more gold than the system can assimilate. Subsequent dose should be withheld or reduced until the reactions have disappeared and the blood count is normal. Skin reactions should be treated with systemic and topical antihistaminics and corticosteroids. If agranulocytosis, thrombocytopenia or aplastic anaemia is diagnosed, immediate injection of dimercaprol, with corticosteroids, androgens and penicillamine orally, must be given. Fresh blood and/or platelet transfusions should be given with reversed barrier nursing pending recovery of the bone marrow.

Contact the Poisons Information Centre for advice on management of overdosage.

**PRESENTATION AND STORAGE CONDITIONS**
MYOCRISIN 10mg/0.5mL, 20mg/0.5mL, 50mg/0.5mL ampoules are available in packs of 10.

Protect from light. Store below 25°C. Solutions which have darkened in colour must not be used.
POISON SCHEDULE OF THE MEDICINE
Schedule 4

NAME AND ADDRESS OF THE SPONSOR
sanofi-aventis australia pty ltd
12-24 Talavera Road
Macquarie Park NSW 2113

DATE OF APPROVAL
Myocrisin PI was Grandfathered and has not been evaluated by the TGA.
Date of most recent amendment: 17 September 2007